AN ANALYSIS of 62 CASES of SYPHILIS with SPECIAL REFERENCE to the EARLY DIAGNOSIS by LABORATORY METHODS.

by

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AN ANALYSIS OF SIXTY TWO CASES OF SYPHILIS, WITH SPECIAL REFERENCE TO THE EARLY DIAGNOSIS BY LABORATORY METHODS.

I. SHORT SKETCH OF THE AETIOLOGY.

Syphilis has always been regarded as an infective disease because of its mode of transmission and the fact that the primary lesion is always situated at the point of contact with a person suffering from the disease.

During the last thirty five years many organisms have been found in syphilitic lesions and suggested as the cause of the disease; practically the only one to outlive its discovery was the bacillus of Lustgarten[1] discovered in 1884, eventually found to be, in all probability, identical with the Smegma bacillus.

In April 1905 Schaudinn and Hoffmann[2] described two types of spirochaetes in a number of syphilitic lesions, - one type strongly refractile, with a thick body - broad coils, and easily demonstrated by staining methods, the other very thin, weakly refractile, with narrow steep coils, not easily stained, in fact seen only after staining with/

with a modified Giemsa's stain.

This latter organism was found in the following syphilitic lesions, primary sores, enlarged syphilitic glands and condylomata. It was named the pale spirochaete or Spirochaete pallida. It was not found in uninfected persons. The former organism was not found in pure syphilitic lesions without mixed infection and was not found constantly, and to it the name Sp. refringens was given. This spirochaete has since been cultivated by Noguchi[3] and according to him it is not pathogenic in animals.

These observations were confirmed by Spitzer[4] who found the Sp. pallida constantly present in a large number of cases of syphilis.

Sobernheim and Tomasczewski[5] found the Spirochaete pallida in fifty cases of primary and secondary syphilis, but failed to find them in eight tertiary cases.

Mulzar[6] who found them invariably in twenty cases of clinical syphilis, failed to find them in fifty six carefully investigated non syphilitic persons.

In tertiary lesions the Sp. pallida has been found less constantly than in primary and secondary lesions, but its presence in gummata has been demonstrated/

demonstrated by Tomasczewski[7] and others.

Noguchi and Moore[8] succeeded in demonstrating the Sp. pallida in the brain of a case of general paralysis.

In 1903 Metchnikoff and Roux[9] succeeded in transmitting the disease to monkeys. They found the anthropoid apes to be the most susceptible. Their results were confirmed by Lassar[10] Neisser[11] Nicolle[12] and others.

Animal inoculations were carried out as follows. Pieces of, or scrapings from, syphilitic lesions in which Sp. pallida could be found, were implanted in the mucous membrane of the genitals or eye, and in twenty six days a typical indurated chancre appeared at the site of inoculation. This was followed by swelling of lymphatic glands, and fifty six days after inoculation by a secondary eruption.

The Sp. pallida were demonstrated both in the primary chancre and in the secondary enlarged glands. No organisms resembling Sp. refringens were found in these animal lesions.

After several attempts, Noguchi[13] succeeded in getting a pure growth of the Sp. pallida by inoculating/

inoculating special media with discharges from syphilitic lesions in man. He produced typical sores in monkeys with the pure cultures thus obtained. Hoffmann[14] also obtained a pure growth of the Sp. pallida direct from a human source, and with it produced typical lesions in monkeys.

II. EARLY DIAGNOSIS BY MEANS OF LABORATORY METHODS.

Until the discovery of the Spirochaete pallida by Schaudinn and Hoffmann in 1905 the organism responsible for the disease was unknown, and the diagnosis of a case of syphilis rested solely on the clinical picture presented.

Not infrequently, before a definite diagnosis could be made and treatment commenced, the case had to be kept under observation until secondary manifestations appeared. This procedure involved the loss of very valuable time and made it possible for a patient in a very infectious condition to mix freely with the community at large, and possibly spread the disease.

Within recent years two laboratory methods have been used to assist the clinician in the diagnosis of syphilis, namely the Wassermann reaction, and the demonstration of the Sp. pallida in the tissues and in the discharges from the lesions.

The/

The Wassermann reaction is an application of the Complement fixation test of Bordet and Gengou[15]. As originally used by Wassermann, Neisser and Brück[16], the antigen was a salt solution extract of an organ of a syphilitic foetus.

Since then many modifications of this reaction have been introduced. The method adopted in this laboratory will be described later.

Unfortunately this reaction does not show itself in many cases of syphilis until secondary manifestations have appeared. It is, therefore, of comparatively little value in the early diagnosis of the disease. On the other hand, in the later stages as a means of diagnosis, and throughout the disease as a control for treatment, the method is of great value.

At first, owing to the difficulty of demonstrating the organism in preparations from primary and secondary lesions, the direct microscopic method was not universally employed.

With the advent of the dark ground illumination method it became possible not only to demonstrate spirochaetes with ease, but also to differentiate certain closely allied forms from one another.

The dark ground illumination method of examination is carried out by means of an ordinary microscope fitted with a special condenser in place of the/

the usual Abbé condenser, and a diaphragm or stop placed in the 1/12th oil immersion lens. The specimen consists of solid particles such as blood cells, bacteria and spirochaetes, and the liquid in which they float. The liquid constitutes a back ground for the solid particles. As a result of the special condenser, the rays which traverse the fluid of the specimen pass on practically without change of direction and reach the cover-glass at such an angle that they escape the microscope: The result is darkness as far as the liquid part of the specimen is concerned. On the other hand, such rays as impinge on solid objects in the specimen are reflected from, or refracted by the latter, and taking a more vertical direction enter the microscope to form brightly illuminated images of these solid objects. (See figures No. 3 and No. 4). The type of Condenser etc. and the method of examination used in this laboratory will be described later.

Harrison[17] thus emphasises the importance of the early demonstration of the Sp. pallida in syhilitic discharges. "After infection the longer the spirochaete is permitted to multiply in the tissues the more serious is the damage which is inflicted on them. Hence it is of the utmost importance that the spirochaete/

spirochaete should be destroyed at the earliest possible moment by employment of energetic anti-syphilitic treatment as soon as its presence has been definitely recognised".

By clinical observations, and by watching the effect of treatment commenced at various stages of the disease on the Wassermann reaction, it is noticed that the cases diagnosed and treated early, respond more quickly to treatment and the results are more lasting than if treatment is commenced at a later date.

Hence, if satisfactory results are to be obtained it is most important that a definite diagnosis be made at the earliest possible moment. With the object of determining the best methods of early diagnosis, exudates from syphilitic sores have been examined by various methods and the results noted.

The methods tested and adopted, and those discarded, along with their respective results will now be described.

III. LABORATORY METHODS.

A. Wassermann Reaction.

5 - 10 c.cs. of blood are withdrawn from a vein of the patient in the usual manner. The serum, separating/

separating from the clot is "inactivated" in a water-bath at 56° C. for thirty minutes.

The Antigen employed is an alcoholic extract of guinea-pigs' heart prepared in the way described in Browning and Mackenzie's book.[18] For use a 1 in 5 dilution in normal saline is employed. A three tier rack (fig. No. 1) for small test-tubes is used, the tubes in the upper and middle tiers containing Antigen in a dose which is ascertained from time to time in the usual fashion.

The lower tier of tubes contains the Serum Control. Inactivated serum is added in the amount of ·1c.c. to the three tubes of each case. e.g.(in fig. No. 1 to tubes 1a, 1b, & 1c.)

The Complement (guinea-pig serum 24 hours old) is titrated, using carefully washed sheep's R.B.C. (1c.c. of a 1% suspension to each tube) and the specific haemolytic serum of a horse as Immune body, taking the dose of I.B. as five times the M.H.D which is found in the same manner as for Complement.

To the upper tier of tubes (patients' and positive control only) 6 M.H.D. Complement are added.

To all the tubes in the middle and lower tiers 3 M.H.D. Complement are added.

At/

At the same time positive, negative, antigen and saline controls are put up.

The dose of Complement in the negative, antigen and saline tubes is 3 M.H.D.

The tubes remain one hour in the dry incubator at 37° C., and at the end of that time 1 c.c. of R.B.C. and I.B. mixture is added to each tube.

The tubes are again placed in the incubator and observed from time to time to ensure that the ingredients are mixing properly. At the end of one hour a reading is taken, and again after standing 12-24 hours in the cold.

If both antigen-serum-complement combinations (tubes 1a & 1b) show no haemolysis a triple plus (+ + +) is given to the case.

If the upper tier tube (2a) shows partial haemolysis and the second tier tube(2b) shows no haemolysis, a double plus(+ +) is given to the case.

If there is complete haemolysis in the upper tier tube (3a) and only partial haemolysis in the second tier tube(3b), the case is regarded either as a single plus(+) or as showing "some fixation" according to degree. Haemolysis of course takes place in the tubes of the lower tier (1c,2c,&3c.)

If/

If the tubes in all three tiers show complete haemolysis the case is a "Complete Negative"(C.N.) (tubes 4 & 5 in fig. No. 1).

This method may be regarded as a slight modification of the one adopted at Rochester Row Military Hospital London,[19] the main differences being that in London, Cholesterin is added to the Antigen, 5 & 3 doses of Complement are employed, and the tubes are placed for half an hour at room temperature before being put in a water bath at 37° C.

B. Dark-ground illumination.

1. Preparation of Microscope, lamp, and slides etc.

The microscope is an ordinary Leitz instrument fitted with a 1/12th oil immersion lens, into which a conical stop is fitted to cut down the aperture of the lens from 1·3 to 1·0, and also a Watson's paraboloidal dark-ground condenser in place of the Abbé condenser. (See fig. No. 3 & 4)

In a Watson's Condenser the central rays of light from the mirror are cut out by means of a circular piece of silver foil placed in the centre of the under surface of the condenser, so that only the peripheral rays pass into the condenser and are reflected as shown in red ink in figure No. 4. Since only the peripheral/

peripheral rays reach the specimen a broad cylinder of light must be reflected from the mirror and this necessitates the use of a powerful lamp.

If a hemispherical dark ground Condenser is used a much weaker light can be employed.

Several methods used to centre the condenser are described by Col. Harrison D.S.O., R.A.M.C.[20] in his book entitled "The Diagnosis and Treatment of Venereal Diseases in General Practice" where also there is a more detailed description of the dark ground illumination, but, as a Watson's Condenser is not fitted with centring screws, the following modified technique is adopted for centring the light and completing the examination.

Place the lamp so that the lens is about 14 inches from the mirror of the microscope, and the light rays strike full on the mirror.

Before fitting the condenser, and before fitting an objective to the microscope, put on a low powered eye piece and pull out the microscope tube. Turn on the light, and look down the microscope from a distance of about 9 inches from the eye piece. An image of the source of light is seen, and by manipulation of the mirror this image is brought into the centre/

centre of the eye-piece diaphragm. Replace the condenser, and screw on a low powered objective and a No. 3 eye-piece.

Mount the slide, applying cedar oil, (free from air bubbles), between the top of condenser and the bottom of the slide. Now examine with a No. 3 objective, and a patch of light will be seen in the field. If this is not in the centre bring it there by manipulating the mirror. If this light appears at first broad and diffuse, or ring-like, and becomes more so when the condenser is racked down, the slide is probably too thick. If it appears small and bri- bright and, on racking down becomes larger and more diffuse, the slide is probably of right thickness.

The condenser is left in that position at which, with the specimen in the focus of the low-power objective, the patch of light in the centre of the field is at its smallest and brightest.

More care has to be taken in focusing a hemispherical condenser than a paraboloidal condenser.

The specimen is now ready for examination with a 1/12th oil immersion objective fitted with a stop (fig. No. 3) and a No. 4 eye-piece.

Place a drop of oil, (free from air bubbles), on/

on the cover-glass, and gently lower till the objective just touches the cover-glass. Then on applying the eye to the eye-piece, and on carefully raising the objective, the correct focus is obtained. Even at this stage it may be necessary to adjust the condenser slightly in order to get a more perfect image. The slides used are about 1/16th in thickness, and the cover glasses are No. 1 size. The lamp is an Argus Arc lamp with a bull's eye lens. The lamp is connected through a resistance coil with the ordinary lighting system. The wiring should be so arranged that the cored or positive carbon lies horizontally, and the solid or negative carbon lies vertically.

The following points are of the greatest importance if reliable results are to be obtained.

1. Centring the condenser and the light.
2. A powerful and steady light is required.
3. Slides and cover-glasses to be of proper thickness.
4. Specimen and cedar-oil to be free from air-bubbles.
5. Not too many red blood cells in specimen (the presence of a few is of assistance in focusing).

B. Continued.

2. <u>Preparation of the patient etc.</u>

1. Primary sore.

The/

The patient is requested to sit on a stool and hold his penis in his hand, displaying the chancre. With a piece of cotton wool held in a pair of dressing forceps the chancre is washed with saline dried and rubbed well with a fresh piece of cotton wool and left for a few minutes, when, in the majority of cases, there will appear on the surface of the ulcer a copious supply of clear exudate.

In certain cases it is necessary to apply digital pressure on two sides of the ulcer a little distance away from the edges, before sufficient fluid appears. With the aid of a capillary pipette a small quantity of exudate is taken up from the edge of the chancre. This exudate is then placed on a cover-glass and a slide lowered on top of it, and gently pressed down.

The slide is then examined as previously described. With a little practice the mirror is easily adjusted and the correct focus found for the examination of the specimen. If the Sp. pallida is found, more exudate is taken up in a capillary pipette and transferred to several other thicker slides for examination by the staining method etc.

If the patient is some distance away, serum may be sent to the laboratory in capillary tubes sealed/

sealed at either end.

In a primary lesion of the penis, which is complicated by phymosis, and as a result with a certain amount of balanitis with thickish yellow discharge, the examination is rather difficult owing to the number of pus cells and other spirochaetes masking the Sp. pallida.

In such cases the following procedure is adopted. Firstly, clean up the mouth of the prepuce with cotton-wool and wait a few minutes. As a rule, a little clear or slightly tinged exudate appears and in this the Sp. pallida may be found. If not, wash out the space under the prepuce with warm sterile saline by means of a small glass syringe. Massage the chancre gently through the prepuce and wait a few minutes. Insert the point of the capillary pipette and guide it as close to the chancre as possible, and from this neighbourhood suck up a little exudate. In the two cases so examined, the Sp. pallida was found. It has been the practice in this hospital, when a patient appears with a chancre which can be felt through the prepuce, or reasonably suspected, to circumcise and expose the sore which can be then readily examined.

2. Enlarged glands.

If/

If material is required from enlarged glands, the method adopted is that described by Harrison.

An assistant fixes the gland between the finger and thumb of the left hand, and pushes it up against the skin, and it is held there with the fingers of the other hand. A hollow needle attached to a sterile syringe in which is a little sterile saline, is then run into the middle of the gland.

The fact that the gland has been punctured successfully can be demonstrated by moving the needle to and fro, when the gland will be felt to move with it.

A few drops of sterile saline are injected into the gland substance and the gland is then massaged. The saline creates for itself a space around the needle-point, and the massage forces spirochaetes into the saline. Suction is then applied by means of the syringe and a little blood stained fluid aspirated. This is examined as described above.

3. Condylomata and Moist papules.

Condylomata and Moist papules are first washed with saline, dried and rubbed vigorously with dry cotton-wool, and the exudate or serum collected in a capillary pipette and treated as in the case of

a/

a Primary Sore.

4. Secondary Rashes.

The specimen is obtained by scraping off the surface of the papule and then applying suction to it. The mouth of an ordinary test-tube is smeared with vaseline and the other end heated gently. The mouth of the test-tube is then firmly applied to the skin so as to encircle the papule, and by cooling the other end of the papule is "cupped" and the serum examined as before.

5. Mucous patches and other lesions within the Mouth.

The aim here is to obtain a specimen as free from saliva as possible, since the saliva may contain a spirochaete (Spirochaete microdentium) which is difficult to distinguish from Spirochaete pallida.

In the fore part of the mouth or lip, dry off the saliva and keep it off by packing round the part with cotton-wool, then rub the patch with dry cotton-wool, removing any crust, wait a little and then take off the exudate in a capillary pipette. If the lesion is on the pillars of the fauces, with the aid of a tongue depressor it is dried with a swab of cotton-wool held in a pair of dressing forseps, and then/

then scraped gently with a small blunt curette and the serum collected in a capillary pipette.

C. Staining and allied Methods.

1. Giemsa's Stain.

A solution said to be Grübler's Giemsa stain was first used, and later, solutions obtained from various sources were used.

a. Films fixed in absolute alcohol for 15 minutes, and dried.

b. Diluted stain - 1 drop stain to 1 c.c. distilled water - placed on film for from 15 minutes to 12 hours.

c. Wash film in distilled water, dry in the air and mount in Canada balsam.

2. Burri's Indian Ink Method.

When it could be obtained "Chin Chin" Indian Ink was used, but now it is almost impossible to get suitable ink. One drop of ink and one or two drops of exudate were mixed on a clean slide and a film spread and allowed to dry in the air.

3. Benians Modification of Burri's Method. (Harrison).

Prepare following solutions.

(a) Congo Red - - - - - - 2 pts.

Distilled water to- 100 pts.

Filter before use.

(b) Hydrochloric Acid - - 1 pt.

Absolute/

Absolute Alcohol to 100pts.

On a perfectly clean slide place a drop of the exudate to be examined and a drop of solution (a) alongside it. Mix the two and spread a film, allow to dry and then flood the slide with solution (b), which is allowed to act for one minute. The background is blue, and the spirochaetes stand out from it as white cork-screws.

4. Modification of Fontana's stain.[21]

1. Film of exudate fixed in 1% Glacial Acetic Acid and 8% Formalin for 3 minutes.

2. Pour off surplus and wash in absolute alcohol, and flame off.

3. Gently heat in 5% Solution Tannic Acid in distilled water for 3-5 minutes.

4. Wash well in tap water and stain with slightly warmed Ammoniated Silver Nitrate Solution. ½-2 minutes. (varies) (To 5% Solution silver nitrate add ammonia solution till the precipitate formed is just dissolved - add a few drops more of silver nitrate solution till precipitate just reappears).

5. Wash in distilled water and dry.

The film should be chestnut coloured. If it is only yellow the staining, from Tannic Acid onwards, should be repeated at once. (from and including No.3)

It has been noticed here that, with certain/

certain samples of tannic acid the film required more heat and longer staining than with other samples, in order to give good results. Slides should not be mounted in balsam but should be examined in neutral cedar-wood oil. Many slides in the series have been stained till the spirochaetes were almost black, so that photographs might be the more easily taken.

IV. METHOD OF CASE TAKING.

It has been my endeavour to get the history of each case as accurately as possible, and with this object the interrogation of the patient was carried out as follows.

Each man was examined privately and was informed that the investigation was of a scientific nature and had nothing to do with his Army record. Each date required was obtained with the help of a calendar, and associating the date with leave, change of camp, or other important incident in his Army history. The following points were chiefly investigated.

1. History of Connections - a. Habit.
   b. Precautions.
   c. Dates and places of last three connections.
2. First appearance of sore or discharge - date

3. Date of Examination - interval since sore appeared.

4. Any appearance of rash etc. if so date.

5. Examination.

   a. Appearance of sore?

   b. Enlarged glands in groin?

   c. Any secondary manifestations?

6. Result of dark ground Examination.

7. Result of stained films.

8a Result of Wassermann R. (the blood being taken on day of examination).

b Result of Wassermann R. after full course of treatment.

9. Sore healed, date etc.

10 Date of Discharge.

In many instances the N.C.O. in charge of the Venereal Department obtained valuable information which assisted me in deciding if the particular history was reliable or not.

I would thus claim for the data obtained from the patients a very considerable degree of accuracy.

As far as this paper is concerned criteria of primary syphilis are as follows.

Cases showing or having shown no secondary manifestations, i.e. rash, general enlargement of lymphatic/

lymphatic glands, mucous patches in mouth or in throat, condylomata etc. In other words primary cases are these in which the infection does not appear to have become generalised. The average age of the chancre when examined in thirty such cases was thirteen days, the youngest being two days and the oldest forty eight days.

V. THE RESULTS OBTAINED BY THE VARIOUS LABORATORY METHODS OF EXAMINATION.

The number of cases in the series, examined as they were admitted to hospital was sixty three. Of these, one was a case of "Soft Sore", the remainder, including a doubtful case, which was considered by the clinicians to be syphilitic but which was never confirmed in the laboratory, were cases of syphilis. In each case a diagnosis of syphilis was eventually made by the Surgeon in charge of the Venereal Department.

A. Wassermann Reaction.

As a positive reaction is given in cases of Frambrosia, Trypanosomiasis, and in some cases of Malaria and Leprosy, it may be mentioned that none of the cases examined suffered or had suffered from any of the above diseases. Table No. 1 gives the results in all the cases of syphilis examined (62) with the exception/

exception of five cases which could not be classified, and which will be treated as "Special" cases.

The Sp. pallida was found in all of the sixty two cases with the exception of two. One of these was the doubtful case; a full description of this case will be given later (case No. 1). The other case showed definite secondary manifestations but the chancre had been treated with calomel ointment prior to examination. (case No. 59).

TABLE NO. I.

Result of Wassermann Reaction in 57 cases of Syphilis. This table includes five cases of re-infection after treatment.

Stage of Disease	No. of cases in group	Positive	%	Negative	%	Some fixation	%
Primary Stage	33	7	21·2	25	75·7	1	3·1
Secondary Stage	24	19	79·2	4	16·6	1	4·2
	57						

In order to exclude the possibility of a false result owing to the inclusion of the five cases of re-infection these were excluded but the results were practically the same (see table No.2).

TABLE NO. 2.

Result of Wassermann Reaction in 52 cases of Syphilis. - Initial Infection. (excluding the five cases of re-infection).

Stage of Disease	No.of cases in group	Positive	%	Negative	%	Some fix-ation	%
Primary Stage	28	6	21·4	21	75	1	3·6
Secondary Stage	24	19	79·2	4	16·6	1	4·2
	52						

TABLE NO. 3.

Result of Wassermann Reaction in the five cases of Syphilis - Re-infection after treatment.

Stage of Disease	No.of cases in group	Positive	%	Negative	%	Some fix-ation	%
Primary Stage	5	1	20	4	80	-	-
Secondary Stage	-	-	-	-	-	-	-
	5						

From Tables No. 1 and 2 it is seen that in the primary stage of the disease the Wassermann reaction/

reaction gives 21% positive and 75% negative, while in the secondary stage the figures are practically reversed viz. 79% positive and 16% negative.

It is now an accepted fact that cases of primary syphilis frequently give negative results but the low percentage of positives found in this series (21·4%) is lower even than the result of Hoehne[22] (38%

If in Table No. 2 the two cases which gave some fixation be added to the positive cases, the percentage of positives is still only 25% in the primary stage, but 83·3% in the secondary stage.

In 329 secondary cases Hoehne[23] found 79·1% showing a positive reaction and Noguchi[24] found 86·6% positive in 120 cases.

The statistics of this paper show therefore that as a means of diagnosis in the Primary stage of the disease the Wassermann reaction is of little value. On the other hand in the secondary stage the result is more constant, and is a fairly reliable index of the presence or absence of active syphilis.

Table No. 4 has been included because it shows that the longer the interval between the first appearance of the primary sore and the taking of the blood for the Wassermann reaction the greater is the chance of a positive result.

In/

In the primary stage over 50% of the cases presented themselves for treatment before the chancre was fifteen days old, when a Wassermann reaction was of little diagnostic value.

In the secondary stage no negative result was found after an interval of thirty five days.

The shortest interval before a positive reeaction appeared was twelve days but there was one case which showed some fixation after an interval of eight days.

TABLE/

TABLE NO. 4.

Result of Wassermann Reaction in fifty two Cases of Primary and Secondary syphilis (initial infection).

Days interval between first appearance of sore and taking of blood for Wassermann R.	PRIMARY			SECONDARY.		
	+	−	some fix.	+	−	some fix.
1-5		2				
6-10		8	1			
11-15	2	3				
16-20		2				
21-25	2	1				
26-30		2			2	
31-35	1	2		5	2	
36-40	1			4		
41-45				2		
46-50		1		2		
51-60				1		1
61-70				1		
71-80						
81-90						
91-100				1		
over 100 days				1		
Uncertain				2		
	6	21	1	19	4	1
		28			24	
TOTAL			52			

The effect of treatment on the Wassermann reaction is marked and this is made use of in the following way, to decide when treatment may be suspended. In the majority of cases after eight injections of mercurial cream intramuscularly and seven injections of Neokharsivan intravenously the result is negative no matter how positive the result was before treatment was commenced. A few cases (5 in series) after such a course of treatment, continued to give more or less strongly positive reactions but these were given potassium iodide for a week, followed by two more injections of Mercury and Neokharsivan with the result that the reaction became negative.

In all cases under treatment a Wassermann reaction is done at the end of the usual course, and if the result is negative (and lesions healed) the patient is discharged, but his blood is tested at intervals of three or six months, and if found positive then, he returns for another course of treatment.

KOLMER[25] in his book "Infection, Immunity and Specific Therapy" thus sums up the effect of treatment on the Wassermann reaction.

"It has been abundantly proved, however, that in syphilis a single negative Wassermann reaction is/

is not sufficient definite evidence that a cure has been effected, for the disease may recur after treatment is discontinued, at least to the extent that the Wassermann reaction re-appears, followed by clinical manifestations.

It is necessary, therefore, that successive examinations be made during a period of at least two years, and off and on during the remainder of life. Recent work indicates that certain strains of Sp. pallida have an apparent selective affinity for the tissues of the central nervous system; the Wassermann reaction with blood serum may be negative, whereas with cerebro-spinal fluid it may be positive.

In cases, therefore, of tertiary syphilis, at least, it is advisable to examine the spinal fluid and continue treatment in case it shows a positive Wassermann reaction.

It is generally agreed that the criteria by which the effects of treatment can best be judged are: -

(1) Continued absence of symptoms

(2) Permanent negative Wassermann reaction".

B. Dark ground illumination.

(1) 57 cases of primary and secondary syphilis/

syphilis were examined by means of the dark ground illumination and the Spirochaete pallida found in 55 cases (96·5%).

Of the two cases giving negative results one was the doubtful case, but considered to be a case of syphilis by the clinical experts. (case No.1)

The other was a case of syphilis with a positive Wassermann but it was discovered that he had been secretly treating the chancre with calomel ointment.

The Sp. pallida was demonstrated in the fluid from the enlarged glands of two cases examined but was not found in two fading roseolar rashes.

(2) Five cases which could not be classified were also examined and the Spirochaete pallida found in all of them. In these five cases the specimens were taken from the following lesions.

3 from Mucous patches in tonsils and fauces.

1 from Mucous patch on inside of lip.

1 from unhealed fistula of penis.

C. Staining Method.

(1) Giemsa.

48 slides (not cases) were examined by this method and Sp. pallida found in 17. In this same/

same series the spirochaete was found in forty slides stained by the silver method.

This method of examination was discontinued for the following reasons.

(1) Poor results obtained compared with other methods.

(2) Even when stained, the spirochaetes were relatively difficult to find.

The poor results may have been partly due to the bad quality of the stain available although it was stated to be Grüblers and the method of staining was that described in Muir and Ritchie's Manual of Bacteriology.[26]

There is no doubt, however, that the Sp. pallida does not easily take on the stain, and therefore as a quick and reliable method of diagnosis it cannot be compared with the Silver method.

2. Burri's Indian Ink Method.

Only four cases in this series were examined by this method and the spirochaete was found in none of them, although the dark ground and silver methods demonstrated them in each case. It ought to be mentioned that the ink used in these preparations was old.

Owing to the difficulty in obtaining a suitable ink, this method was given up.

3./

3. Benian's Modification of Burri's Method.

The method was carried out exactly as described in Harrison's Book but the results were not satisfactory and it was discarded.

Twelve cases were examined, with positive results in four. In this same series the spirochaete was demonstrated both by the dark ground and the silver methods.

4. Modification of Fontana's Silver Stain.

(1) Fifty seven cases of Primary and Secondary Syphilis were examined by this method and the Spirochaete pallida found in forty three cases (75·4%

In many of the negative films spirochaetes were found, but the effect of the heating etc. had so distorted them that it was impossible to say whether or not they were Sp. pallida.

As the examination of the series of cases was commenced about the same time as the stain was adopted, the comparatively low number of positive results may be due to the fact that the earlier technique may have been slightly defective. If care is taken this method shows up the Sp. pallida well and its morphological characters can be studied fairly accurately.

(2) Five "special cases were also examined and/

and the Sp. pallida demonstrated in four of them.

VI. COMPARISON OF RELATIVE VALUE OF THE TWO MICROSCOPICAL METHODS OF EXAMINATION ADOPTED.

This question has been dealt with from the following points of view.

(1) Certainty of correct diagnosis.

(2) Time occupied in making the diagnosis.

(3) General considerations.

1. Certainty of Diagnosis.

TABLE/

TABLE NO. 5.

57 cases of Primary and Secondary Syphilis examined.

Stage of Disease	No. of Cases	Dark ground illumination				Silver Method.			
		Sp. pallida found	%	Sp. pallida not found or doubtful.	%	Sp. pallida found	%	Sp. pallida not found or doubtful.	%
Primary	33*	32	97	1	3	23	70	10	30
Secondary	24+	23	95	1	4·2	20	83·5	4	16·5
Total	57	55	96·5	2	3·5	43	75·4	14	24·6

* Includes a doubtful case with negative results.

\+ Includes a case in which lesion was being treated with calomel. - negative result.

In the above table the percentage of total positive results in dark ground series is 96·5% and in the silver series 75·4%. If the doubtful case and the case which was treating the chancre secretly be excluded, the percentage of positive results in the two methods would then be dark ground illumination 100% silver method 79%.

From the results obtained here the dark ground Method is much superior to the silver method as a means of diagnosing syphilis,

Phillip and Glynn[27] found the Sp. pallida by the dark ground method in 100% of the thirty one cases examined.

2. Time occupied in making the diagnosis.

The time taken in preparing the patient is equal in both cases as the process is the same in each instance. The making of the film for dark ground method is so simple that very little time is taken. On the other hand in the silver method the film has to be spread, dried, fixed, and stained, and this will take from twelve to thirty minutes.

Time expended in examining the films

Dark ground illumination.

In all cases where found, the Sp. pallida was seen in the first film examined except in one case/

case where three films were examined. (See Table No.6 at end of paper).

In the majority of these cases the Sp. pallida was seen at once, and in no case did it take longer than three to five minutes to find it.

Silver Method.

In the forty three cases where found, the Sp. pallida was seen in the first film on thirty nine occasions and in the second film on four occasions.

In only a few instances was the Sp. pallida found at once in the stained film and in many cases a search of from ten to fifteen minutes had to be made before finding it. It has to be remembered that in the case of the dark ground method the film is of limited area and comparatively thick, while in the silver method the film is spread out over a large area and is thin, so that more time must be spent in searching a silver film. This in my opinion only partly explains the finding of relatively few spirochaetes in stained specimens when in specimens taken at the same time and examined by the dark ground method the spirochaetes are quite numerous.

The dark ground method is therefore a much quicker method of making a diagnosis than the silver method.

3. General Considerations.

The/

The dark ground method of examination is undoubtedly the best method for distinguishing the various types of spirochaetes as they are examined in their natural media and not distorted by fixing, heating etc., and most important of all, their movements can be followed. Again, as the films require no treatment the chances of error in technique are nil as compared with the staining method.

On the other hand, no permanent specimens can be made with dark ground films.

The silver method is very good for making films for purpose of photography. It has been found that films, treated with the silver method and giving excellent results in some cases, tend to fade, and these same films if examined after a few days show practically no spirochaetes. On restaining, the spirochaetes are easily seen but the differentiation is not so good as in the first instance.

Therefore films treated with this method must be examined within twenty four hours of staining. As a means of demonstrating spirochaetes this silver method is very good but its use would be much enhanced if some means could be adopted for fixing the silver albuminate and so making permanent specimens.

VII./

VII. THE SPIROCHAETE PALLIDA AND OTHER SPIROCHAETES WHICH MAY BE FOUND IN SYPHILITIC LESIONS.

A. The Spirochaete pallida.

The Sp. pallida is an extremely fine spirally twisted thread-like organism, but differing from other spirochaetes in its marked slenderness, its regular and close spirals, and its difficulty in staining.

When examined in the living condition by means of the dark ground method its movements, which are very characteristic, in fact diagnostic, can be studied. These movements are:-

(1) cork-screw-like rotation on its long axis,

(2) bending and lashing and

(3) slow progression.

It is by means of this rapid corkscrew-like movement that it glides slowly forward, and it has been noticed in this laboratory that this screw-like action is often suddenly reversed, with the result that the organism stops and proceeds backwards.

In other words, at first the spirals which may be revolving from left to right stop, and begin to revolve from right to left. Its rate of progression is relatively slow and in this it differs from most/

most other spirochaetes.

Its flexibility is marked. In some specimens it may bend so as to form a circle or as is most common it may bend suddenly at one point and form a letter L. Again in other specimens one part may remain rigid and the other lash about vigorously. The Spirochaete pertenuis of "Yaws" is the only other spirochaete which can compare with it in flexibility and as this disease is confined to certain tropical regions it is of little practical importance here.

Another characteristic feature when examined by the dark ground method is its extreme whiteness as compared with the glistening or refractile appearance of the other spirochaetes.

If the objective of the microscope is raised a little the Sp. pallida remains white but the other spirochaetes show a reddish tinge. (Harrison). It varies in length but the average length is about 8-10 microns.

The number of spirals to a given length is of diagnostic value.

If seen alongside a red blood cell, the diameter of which is 7·5 microns, it will be noticed that there are seven coils to the width of the red cell. (See photographs Nos. 1 and 2).

Very/

Very long forms have been seen but generally they show definite thinning out at one or two places as if they were going to divide into two or three single forms. It is often at such a point that the bending occurs especially if the spirochaete is of the longer variety. It has also been noticed in this laboratory that after several injections of Neokharsivan and Mercury the Sp. pallida becomes less active, less regular and has a shrunken appearance.

B. Other spirochaetes which may be found in lesions of the genitals are: -

(1) Sp. refringens.

(2) Sp. gracilis and

(3) Sp. balanitidis.

The above are all surface spirochaetes and are not found deep in the tissues like the Sp. pallida. Hence the reason for washing and rubbing the chancre vigorously and so getting the serum from the deeper tissues for examination.

1. Sp. refringens is easily distinguished. It is a large thick wavy spirochaete with few wide spirals to a given length and it moves over the field quickly. (See photo. No. 6). In stained specimens it tends to loose its wavy spirals and become straightened out.

Noguchi[28]/

Noguchi[28] has cultivated the spirochaete by inoculating a special media with the discharge from a condyloma. In culture it differs from Sp. pallida in that no fresh tissue need be added to the media and in that so far the growth has proved non-pathogenic for animals.

Sp. refringens was found in fifteen of the fifty six lesions on genitals examined and in the majority of these they were found in chancres in or near the coronal furrow.

2. Sp. gracilis.

The Sp. gracilis was described in 1909 by Levaditi and Stanesco[29] and found by them in syphilitic and non-syphilitic lesions occurring in human genitalia.

It is about twice as thick as Sp. pallida and is more actively motile but does not show the degree of flexibility of pallida.

It has regular close coils but to a given length, say the diameter of a red blood cell, there are only five coils compared with seven in the case of pallida. According to Levaditi and Stanesco it is non-pathogenic for monkeys. This spirochaete is very liable to be mistaken for pallida and therefore careful attention must be paid to the following points./

points.

(1) Glistening appearance - not the dead white appearance of pallida.

(2) Rusty tinge if focus is altered.

(3) Rate of movement across the field.

(4) Amount of flexibility.

(5) If red blood cells are in the field - note the number of coils (5) in that length of spirochaete which is equal to the diameter of a red cell.

(6) Twice as thick as pallida.

The Sp. gracilis was found in four cases of this series.

3. Spirochaete balanitidis.

(a) Harrison[30] describes a spirochaete which he calls Sp. balanitidis with the following morphological characters.

A short thick spirochaete with two or three coils in its whole length.

It is so active in its movements that it is only kept on the field with difficulty.

It is easily distinguished.

Two other authorities quoted below describe spirochaetes which they term Sp. balanitidis but none of which are likely to be mistaken for Sp. pallida.

(b) Hoffmann and Prowazek[31] in 1906 described/

described a spirochaete which they called Sp. balanitidis.

Its chief characters are.

A strongly refractile spirochaete with regular, wide coils and 10-12 microns in length.

This spirochaete has not been seen in any of the cases examined.

(c) Levaditi and Stanesco[32] in 1909 described a spirochaete which they called Sp. balanitidis

It is a large spirochaete with wide undulations, rounded extremities and one terminal flagellum.

It is very active.

This spirochaete has not been observed in any of the cases examined.

There is some dubiety as to what exactly is the Sp. balanitidis. That described by Harrison is a totally different organism from that described by Hoffmann and Prowazek or that described by Levaditi and Stanesco. In this series of cases Sp. balanitidis as described by Harrison has been found in seven cases of which three showed balanitis more or less marked (see photograph No. 8). The other four cases showed no signs of balanitis.

(c) Other spirochaetes found in Mouth and Throat lesions.

(1)/

(1) Sp. microdentium.

Noguchi[33] in 1912 described the spirochaete and succeeded in cultivating it in special media. It is less than ·25 microns in thickness, varies in length, tapers towards either end, and has sharp closely set coils. It is actively motile and is more like Sp. pallida than any other spirochaete likely to be met with in this country.

It can only be distinguished from pallida with great difficulty. The main points of difference being.

(1) It is not so flexible.

(2) It is more dazzling - not white.

(3) It shows the rusty tinge when focus is altered.

I have never been able to satisfy myself that I have found one of these spiroshaetes. In two of the three lip chancres examined, (one included in in this series) after washing the lip carefully with saline, drying and rubbing vigorously with cotton-wool, spirochaetes morphologically indistinguishable from pallida were found in two cases. Both these cases presented ulcers with marked induration and enlargement of the submaxillary glands and were clinically diagnosed syphilis. In the third case, a doubtful/

doubtful one, no spirochaetes were found.

The only means we have at present of excluding as far as possible an error in diagnosis on account of the Sp. microdentium, is to remove all spirochaetes from the surface by washing with saline and Methylated Spirit and then waiting for fresh serum to exude from the deeper layers of the tissue.

The possibility of a mistake is greater when Sp. microdentium is found than when Sp. pallida is found.

(2) Sp. macrodentium.

Noguchi[34] cultivated this spirochaete from a case of ulcerative stomatitis.

It is a larger spirochaete than either Sp. microdentium or Sp. pallida and shows fewer and wider coils. It also shows less motility than either of the above. It is easily distinguished from Sp. pallida. This spirochaete has not been observed in any of the cases examined here.

(3) Spirochaetes of Vincent's Disease.

These spirochaetes are large, with few wide coils or undulations and are always associated with a definite fusiform bacillus. They are easily distinguished from Sp. pallida (see photographs/

photographs Nos. 9 and 10).

These spirochaetes have been obtained in pure culture by Ellermann,[35] Weaver and Tunnicliff,[36] and Mühlens[37] who found they produced the odour characteristic of pyorrhoea alveolaris. This spirochaete was found in one case in the series, (case No. 14), which had a syphilitic throat lesion complicated by Vincent's disease. No difficulty was experienced in distinguishing the two spirochaetes when examined by the dark ground or silver method.

D. Spirochaetes met with in lesion of the lips.

The spirochaetes found in lesions of the lips are the same as in mouth lesions but Sp. microdentium is the most important.

E. Other structures which may be taken for spirochaetes in dark ground preparations.

In specimens which contain much blood, fine hair-like filaments are sometimes seen wriggling across the field. At times they appear as a row of shining dots. With care they are easily distinguished from spirochaetes, but if the examination is hurried, mistakes are liable to occur.

VIII./

VIII. BRIEF SUMMARY OF FIVE "SPECIAL" CASES.

The following cases were called "special" cases because they presented unusual clinical facts.

CASE NO. 13.

DOUBTFUL RE-INFECTION OR "PERSISTING CHANCRE".

(Hutchinson) Age 23.

Incubation period. 19-20 days.

Admitted Military Hospital - Ireland 1/10/17 with sore on under surface of glans.

Wassermann reaction not known.

Given seven doses "606", each dose ·4 grammes, and 9,1 gr. doses of Mercurial Cream.

Finished treatment 8/12/17 and was discharged on 10/12/17 with ulcer still unhealed, and according to patient, with a fistula leading into urethra about ⅓" from meatus.

Admitted here 9/2/18 (2 months later).

Condition as above but with a small ulcer at side of opening into urethra. No secondary manifestations.

D.G.I. Two Sp. pallida found in serum from ulcer.

Silver. Sp. pallida found.

Wassermann/

Wassermann R. 15/2/18 Complete Negative.

Treatment. Mercury 7,1 grain doses.

Neokharsivan (3,·6 grammes
(3,·9 grammes.

Wassermann R. 29/3/18 Complete Negative.

Sore never healed.

Discharged 6/4/16.

Comments.

This case was most probably a Re-infection after treatment in Ireland, but it may be a case similar in some respects to the cases described by Hutchinson[36] in his book on Syphilis, where he cites several cases with "persisting chancres".

It is worth noting that the Sp. pallida was found in the ulcer within two months of the patient having had a complete course of treatment.

CASE NO. 14.

SECONDARY THROAT LESION COMPLICATED BY VINCENT'S DISEASE. Age 22.

Incubation period. 34 days.

Sore in prepuce noticed while in Fever Hospital with Diphtheria.

Discharged Fever Hospital and admitted to this Hospital 14/11/17.

Diagnosed Syphilis but transferred to another Hospital where Wassermann test (24/12/17) was Complete Negative, but given four doses of"Galyl" and five doses Mercury.

Diagnosed "Soft Sore" there and Wassermann (15/12/17) again negative.

Discharged there 19/12/17.

Readmitted here. 8/2/18 with ulcerated left tonsil and whitish plaques in pillars of fauces from which situations specimens were taken. Old hard scar on penis noticed.

Secondary manifestations.

(1) General enlargement of lymp. glands.

(2) Remains of syphilitic rash in arms.

(3) Throat lesion.

D.G.I./

D.G.I. Bacillus Fusiformis and large spirochaete of Vincent's angina also several Sp. pallida found.

Silver Stain. Several Sp. pallida found - readily distinguished from the larger organism of Vincent's disease.

Wassermann reaction. 8/2/18 C. Negative.

Treatment:-

5 doses Neokharsiven

6 doses Mercury.

Throat lesion cleared up after three injections of each.

Wassermann R. 22/2/18 C. negative.

Discharged. 6/4/18.

Comment.

This was a case of Secondary syphilis with a marked throat lesion which was complicated by Vincent's angina and in which both spirochaetes were found.

CASE NO. 15.

"RE-INFECTION OR RELAPSE". Age 27.

Had syphilis in Gibralter in 1914 and there had two doses "606" and nine doses of Mercury.

Denies all subsequent possibilities of infection.

Admitted here 8/2/18 with a mucous patch spreading over soft palate from pillars of fauces.

No primary lesion or scars to be seen.

Other secondary manifestations:-

General enlargement of lymph. glands.

D.G.I. Several Sp. pallida found.

Silver stain. Sp. pallida found.

Wassermann R. 8/2/18 + + +.

Treatment:-

5 doses Mercury &

6 doses Neokharsivan.

Throat lesion healed after second injection of both.

Wassermann R. 7/3/18 +.

Two more doses of Mercury and Neokharsivan given.

Wassermann R. 23/3/18 Complete Negative.

Discharged/

Discharged 28/3/18.

Comments.

This is most likely a re-infection the patient not reporting his primary lesion.

CASE NO. 32.

RELAPSE AFTER TREATMENT WITH "GALYL". Age 25.

Incubation period. Uncertain.

In March 1917 hard chancre noticed.

Given 3 injections into vein (? drug) privately in April 1917.

Wassermann R. June 1917. + +.

In June, July and August 1917 given complete course of "Galyl" and Mercury in London.

Examined here. 5/3/18 and presented one Mucous patch on inside of lower lip and another at angle of mouth on left side.

Other Secondary Manifestations.

Glands in posterior triangle of neck enlarged and shotty.

D.G.I. Sp. pallida found.

Silver Stain. Sp. pallida found.

Wassermann R. 5/3/18. + + +

Treated privately.

Comments.

This is undoubtedly a relapse after treatment with "Galyl", as the patient was quite definite/

definite that he had had no possibilities of re-infection. This history is probably correct as he had been fully occupied with military duties overseas. Interval since his discharge from hospital was 196 days.

CASE NO. 34.

RE-INFECTION AFTER AN INTERVAL OF TEN YEARS. Age 35.

History of syphilis in 1908 when in Navy and was then treated with "pills".

Admitted here 8/3/18 with definite secondary manifestations. - Denied re-infection.

(1) Both tonsils ulcerated and with whitish plaques on anterior pillars of fauces.

(2) Small, moist, papules on scrotum.

(3) Commencing Condyloma of anus.

(4) General enlargement of lymph. glands.

(5) Shotty glands in posterior triangle of neck.

D.G.I.

(1) From throat. Sp. pallida found.

(2) Condyloma. Sp.pallida found.

Silver Stain.

(1) Sp. pallida doubtful.

(2) Sp. pallida found.

Wassermann R. 8/2/18 (+ + +).

Treatment. 7 doses Mercury and 7 doses of Neokharsivan.

Sores healed after second injection of both/

both (21/3/18).

Wassermann R. 20/4/18 Complete Negative.

Discharged 3/5/18

Comment.

This is probably a case of re-infection as it is most unlikely that secondary manifestations would show themselves ten years after the original infection.

IX. SUMMARY OF TEN CASES OF SPECIAL INTEREST.

CASE NO. 1.

CASE IN WHICH NO SP. PALLIDA FOUND. Age 18½.

Incubation. 8-10 days.

Admitted 16/1/18. Sore ¼" diameter on anterior end of prepuce. Edges hard and raised - prepuce swollen and could not be retracted. Discharge from Methia - gonorrhoea.

No secondary manifestations.

D.G.I. No. Sp. pallida found. 8 examinations.

Silver Stain. No Sp. pallida found.

One gland in groin enlarged and skin over it red and tense.

Gland punctured. Numerous polymorphs but no spirochaetes found.

Wassermann R. 17/1/18 C. negative.

Treatment. Circumcised 20/1/18. section made and examined by pathologist with following report

"Ulcer with granulation tissue. Floor infiltrated with cells - polymorphs and mononuclears. Fairly acute inflamation - No giant cells - a little amount/

amount of periarteritis".

6 doses of Mercury and 7 doses of Neokharsivan.

Wassermann R. 23/2/18. C. Negative.

Completely healed 25/2/18.

Discharged 27/2/18.

Comment.

This was probably a case of "Soft sore", but may have been incubating syphilis at the same time. According to the results of D.G.I. it was not a case of syphilis but as the clinical Medical Officer in charge, believed it to be a case of syphilis treatment was commenced at once.

If this was a true syphilitic infection it is the only case of the series which was not diagnosed by the dark ground method.

A positive diagnosis was made on the basis of a hard indurated sore on the penis.

Treatment was begun so early (2nd day) that the negative finding of the dark ground illumination is not surprising.

CASE NO. 28.

CASE OF "SOFT SORE". Age 28.

Incubation period. 8-9 days.

Admitted 26/2/18 - 8 days after the two little ulcers appeared. Two little ulcers, one on prepuce, the other on the glans.

Edges undermined - a little yellowish pus when crusts removed. No marked induration noticed.

Secondary manifestations - Nil.

D.G.I. No Sp. pallida found.

Silver Stain. No Sp. pallida found.

Wassermann 1/3/18 Complete Negative.

Treatment. Local treatment for sores consisted in washing in sterile water and sterile dressings applied.

Sores healed within four days.

Discharged 8/4/18.

Comments.

This was a case of "Soft Chancre". Patient was kept under observation for six weeks in hospital and has reported once (28/5/18) since his discharge from hospital when no symptoms or manifestations/

manifestations of syphilis had appeared. Ducry's[39] bacillus was not found.

The Special Committee of the Medical Research Committee[40] find no evidence that what is clinically known as "soft sore" is a specific disease induced by a special of micro-organism. They recommend that a diagnosis of "soft sore" be founded on clinical evidence, and this only after syphilis has been excluded by observation extending over a period of twelve weeks.

CASE NO. 59.

CASE OF SYPHILIS CONFIRMED BY WASSERMANN REACTION BUT NOT BY DARK GROUND ILLUMINATION. Age 30.

Incubation. 15-16 days?

Admitted 5/6/18. - sores 30 days old.

One sore on fraenum and the other on skin of prepuce.

Beyond slight enlargement of glands of neck (posterior triangle) there were no secondary manifestations.

D.G.I. No Sp. pallida found.

Silver Stain. No Sp. pallida found.

Wassermann R. 11/6/18. + (positive).

Comment.

This patient was transferred before treatment was completed but it was discovered that he had been in the habit of rubbing calomel ointment into chancre every evening and so making the finding of spirochaetes impossible. This is the second case in which the Sp. pallida was not found in a film examined by the dark ground method.

CASE NO. 60.

"CHANCRE" OF LIP. Age 27

An officer when in a hospital in England recovering from a wound, was smoking a cigarette which stuck to his lip; on tearing it away he pulled a piece of skin from his lower lip. From that time the crack in his lip remained open and at one time it became septic.

The above happened about six weeks before admission to this hospital.

The patient was seen by a skin Specialist who recommended that he should have the small ulcer examined by microscopic methods as it looked very like a chancre.

Examination. Ulcer on lower lip about one inch in diameter, was covered with a dry crust towards outer side and towards inside of mouth there was a whitish film of dead epithelium. There was marked induration of tissues round the ulcer, and the submaxillary glands were enlarged and shotty.

No secondary manifestations.

D.G.I. 3 or 4 Sp. pallida found.

Silver Stain. No Sp. pallida found.

Wassermann/

Wassermann R. (before treatment) Complete Negative.

Treatment. 7 doses of Mercury

7 doses of Neokharsivan.

Ulcer healed after two doses of each.

Wassermann. After treatment. C. Negative.

Comment.

A case of accidental infection of crack on the lower lip in which the Sp. pallida was found. The lip was well washed with saline and the mouth shut off with cotton-wool before the serum was taken for examination.

Considering the clinical appearances and history. the presence of a spirochaete indistinguishable from the Sp. pallida, after carefully washing and removing all trace of saliva, decided the question of diagnosis.

CASE NO. 63.

"CHANCRE" TWO DAYS OLD. Age 23.

Incubation period about 40 days.

Sore appeared as small pimple two days before admission to Hospital.

Examination showed small sore on inside of prepuce on dorsal aspect. Size ¼"x 1/8th". It was covered with a hard crust of dried serum. No induration of tissue. Crust removed by washing with saline and bloody exudate examined.

D.G.I. Many Sp. pallida found.

Silver Stain. Many Sp. pallida found. (photo No.2)

Wassermann R. C. Negative.

Case transferred to another Hospital for treatment.

Comment.

This is certainly the earliest case which has been examined. The sore was only two days old and the spirochaetes were more numerous than in any specimen examined previously. There was no clinical evidence that it was a chancre beyond the fact that it had appeared after an interval of about forty days.

In fact the case presented so little evidence of its possibly being syphilitic in origin, that it was almost not examined at all.

FIVE CASES OF RE-INFECTION AFTER TREATMENT.

CASE NO. 6. Age 21.

First infection May 1917.

Incubation about 6 weeks.

Admitted to Hospital in France August 1917 with:-

(1) Balanitis - hard sore under prepuce.

(2) Roseolar rash.

(3) Inguinal glands and anterior cervical glands enlarged.

(4) Throat congested.

Treatment:-

7 doses Mercury.

8 doses Neosalvarson.

Wassermann R. 5/10/17. C. Negative.

Discharged 10/10/17.

Re-infected. January 1918.

Incubation period. 18-20 days.

Admitted here 29/1/18. with chancre in glans penis.

No secondary manifestations.

D.G.I. Many Sp. pallida found.

Silver Stain. Sp. pallida found.

Wassermann R. 1/2/18 C. Negative.

Treatment/

Treatment:-

6 doses Mercury.

7 doses Neokharsivan.

Sore healed after one injection of each.

Wassermann R. 2/3/18 C. Negative.

Discharged. 6/3/18.

Comment.

A case of re-infection after treatment with Neosalvarson and Mercury.

114 days interval between discharge from hospital and the appearance of the second sore.

CASE NO. 8. Age 23.

This case had a similar history to the previous case and was also treated with Neosalvarson in France.

The only difference from the previous case was the fact that the Wassermann reaction gave a positive (+ + +) result on admission here.

The interval between discharge from hospital and re-infection was 179 days.

CASE NO. 16. Age 22.

Infected August 1917.

Incubation 6-7 weeks.

Spirochaete pallida found in a gland in the groin.

Treatment 7 doses Mercury and 7 doses "Galyl"

Wassermann R. 28/11/17. C. Negative.

Re-infected January 1918.

Incubation 37 days.

Chancre on penis - no secondary manifestations.

D.G.I. Many Sp. pallida found.

Silver Stain. Many Sp. pallida found.

Wassermann. Complete Negative.

Treatment 6 doses Neokharsivan and 6 doses of Mercury.

Sore healed after one injection of each.

Wassermann. Complete Negative.

Discharged 21/3/18.

Comment.

A case of re-infection after treatment with "Galyl" and Mercury. The interval between discharge from hospital and re-infection was 73 days.

CASE NO. 23. Age 22.

Infected July 1917.

Treated in a General Hospital July 1917 and had a full course of Mercury and "Galyl".

Discharged 22/10/17.

Re-infected January 1918.

Incubation. 27 days.

Chancre left side of prepuce.

No secondary manifestations.

D.G.I. Many Sp. pallida found.

Silver Stain. Several Sp. pallida found.

Wassermann R. 1/3/18 C. Negative.

Treatment. 6 doses Mercury.

5 doses Neokharsivan.

Sore healed after second injection of both.

Wassermann R. 23/3/18 C. Negative.

Comment.

A case of re-infection after treatment with Mercury and "Galyl". The interval between discharge from Hospital and re-infection was 115 days.

CASE NO. 31. Age 32.

Patient said he had syphilis in 1906 (twelve years ago) and was treated in Plymouth Naval Hospital with ten or twelve intramuscular injections of Mercury.

Re-infection January 1918.

Incubation. 30 days.

Two chancres on inside of prepuce.

No secondary manifestations.

D.G.I. Sp. pallida found.

Silver Stain. Sp. pallida found.

Wassermann R. 6/3/18 C. Negative.

Treatment. 7 doses of Mercury and 6 of Neokharsivan.

Sore healed after second dose of Neokharsivan. and third dose of Mercury.

Discharged. 17/4/18.

Comment.

A case of re-infection after an interval of twelve years and after treatment with Mercury at the time of first infection.

X. SHORT SKETCH OF TREATMENT CARRIED OUT IN THIS HOSPITAL.

The employment of the Arsenical compound "Salvarson" or 606, introduced by Ehrlich in 1909, has been discontinued because of the difficulties connected with its preparation for injection.

"Neosalvarsan" or 914 has since replaced it as a therapeutic agent.

"Neo-Kharsivan" is the name given to a chemically equivalent product placed on the market by a well known firm of manufacturing chemists and is the arsenical compound used in this hospital.

The following is the routine course for ordinary fresh cases of syphilis.

The course is interrupted in the event of dermatitis, jaundice, or other signs of intolerance supervening.

Each patient is carefully watched for signs of stomatitis or general malaise, his weight taken, and his urine tested for albumen before each injection.

Day of Treatment	ARSENICAL PREPARATION — Intravenously: Neokharsivan (914)	MERCURY — Intramuscularly: Mercurial Cream. (given 2 dys after Neokharsivan).
1st	·3 or ·6 grammes	grain 1
8th	·3 or ·6 grammes	" 1
15th	·3 or ·6 "	" 1
22nd	- -	" 1
29th	·4 or ·9 "	" 1
36th	·4 or ·9 "	" 1
43rd	- -	- -
50th	·4 or ·9 "	" 1
57th	·4 or ·9 "	" 1
59th	Blood test (Wassermann)	
	if result is positive or doubtful continue	
	as below.	
61st-77th	Course of Potassium Iodide grains X to XX	
	three times a day.	
82nd	·6 or ·9 grammes	
92nd	·6 or ·9 grammes	

If the blood is negative on the 59th day treatment is suspended. In all cases where practicable blood tests are repeated at intervals of three months at first, and later every six months.

Preparations of Solutions and Method of Injection.

The Neokharsivan is made up in sealed glass ampoules and is a fine yellow powder. The ampoules contain either ·3 ·4 ·6 or 9 grammes.

Sterlized flasks, each containing 20 c.c. of sterile distilled water are then placed in a water bath and brought up to blood heat.

Immediately before injection the contents of one ampoule are dissolved in one of these flasks and are then sucked up into a 20 cc. "Record" syringe with glass barrel. The patient is sitting, his arm is placed on a table, and the skin over a prominent vein is sterilized with ether. A rubber band is then put on the upper arm and held there by an attendant. A sterilized hollow needle which fits the syringe is now plunged into the vein, and when blood flows freely, the syringe is fitted on, taking care that no air-bubbles reach the vein, and the contents slowly injected, the rubber band having meanwhile been removed.

Careful attention is paid during injection to the area round the needle to see that there is no infiltration of the solution into the soft tissues.

The local treatment consists in keeping the lesions clean and washing them daily with a weak Mercurial/

Mercurial lotion.

Treatment of Syphilis (Continued).

Tertiary cases with symptoms are usually treated as shown above from the 1st to the 39th day, and then, if practicable, put on a course of Mercury and iodides.

With the combined Neokharsivan and Mercury treatment, as far as we know no relapses have so far occurred at this hospital, but sufficient time has not yet elapsed for definite conclusions to be drawn. Certainly the lesions heal up remarkably quickly with this method of treatment.

"Galyl", a French preparation introduced in 1913, was used here for many months, but its use was discontinued at the end of last year on instructions from "Central Authority". With this drug the lesions also healed up rapidly but definite relapses have occurred.

XI. INCUBATION PERIOD.

In twenty cases, where reliance could be placed on the history, the question of the incubation period was gone into very carefully, with the result that the average period was found to be 28 days.

The shortest period was eighteen days and the/

the longest forty days.

XII. SUMMARY OF RESULTS OBTAINED IN THIS INVESTIGATION.

(1) Total number of patients examined 63

Definite cases of syphilis	60
Cases of syphilis complicated by treatment	1
Doubtful cases of syphilis	1
Case of "Soft sore".	1
	63

(2) Wassermann reaction results in fifty two cases of initial syphilis infection.

(a) Primary Stage (28 cases) 25% positive

(b) Secondary Stage (24 cases) 83% positive

(c) In the secondary stage no negative result was found in cases where the initial lesion was more than 35 days old.

(d) The earliest positive result was in a case with an initial lesion twelve days old.

One case gave "some fixation" when lesion was eight days old.

(3)/

(3) Dark ground illumination results.

(a) Sp. pallida found in 100% of the sixty definite cases of syphilis.

(b) It was not found in the case complicated by local treatment or in the doubtful case.

(c) It was found in the fluid of enlarged glands in the two cases thus examined

(d) It was not found in the two fading roseolar rashes examined.

(4) Staining Method.

(A) Giemsa.

(a) Sp. pallida found in 35% of the 48 slides thus examined.

(b) This method discontinued.

(B) Burri's Indian Ink Method and Benian's Modification.

Results unsatisfactory for reasons given previously.

(C) Modification of Fontana's Silver Stain.

(a) Sp. pallida found in 79% of the 60 definite cases of syphilis.

(5) The Spirochaete pallida and other spirochaetes found in syphilitic lesions.

(a) As far as I am aware the only original/

original observations made in regard to the Sp. pallida are as follows.

(1) In pallida the corkscrew-like movement, by means of which it glides forwards, is at times suddenly reversed with the result that the organism stops and retraces its steps. This changing of direction of the spiral movement is frequently rapidly repeated, and produces the result, which is often noticed, of a spirochaete showing great activity, but covering very little ground.

(2) After two or three injections of Neokharsivan and Mercury the Sp. pallida becomes less active, less regular and has a shrunken appearance.

(b) Sp. refringens found in 27% of the 56 genital lesions examined.

(c) Sp. gracilis found in four cases.

(d) Sp. balanitidis found in seven cases.

(e) Sp. of Vincent's disease found in one case in which also the Sp. pallida was found.

(6) Cases of interest.

(a) Doubtful re-infection or "persisting chancre" (Hutchinson).

(b) Secondary throat lesion complicated by Vincent's disease.

(c) Doubtful re-infection or relapse.

(d) Definite relapse after treatment with "Galyl".

(e)/

(e) Case of "soft sore".

(f) Chancre of lip.

(g) Early chancre.

(h) Five cases of re-infection after treatment.

(7) Treatment. Its immediate effect.

(a) In the majority of cases the lesions heal up after two or three injections of Neokharsivan and Mercury.

(b) In the majority of cases the Wassermann reaction is negative after seven injections of Neokharsivan and eight injections of Mercury.

(8) Incubation period.

(a) Average incubation period found to be 27 days.

(b) The shortest period was 18 days.

(c) The longest period was 40 days.

XIII. GENERAL SUMMARY OF CONCLUSIONS.

(1) The demonstration of the Spirochaete pallida in the exudates from suspected syphilitic lesions is the surest evidence of such lesions being syphilitic in nature.

N.B. The specimen must be taken from the actual lesion, not simply from its neighbourhood.

(2) Dark ground illumination is the best method of examination, for the following reasons.

(1) Reliability.

(2) Simplicity.

(3) Rapidity.

The following points are of the greatest importance if reliable results are to be obtained,

(1) Centring the condenser and the light.

(2) A powerful and steady light required.

(3) Slides and coverglasses of proper thickness.

(4) Specimens and cedar oil must be free from air bubbles.

(5) Not too many red blood cells in specimens - the presence of a few are of assistance in focusing.

(3) The modification of Fontana's Silver Method appears to be more reliable than any of the other staining or allied methods.

One/

One disadvantage of this method is that the film thus treated tends to fade and therefore must be examined within 24 hours of its preparation.

Such a film can, however, be restained with success, but the differentiation is not so well marked as in the first instance.

Films of exudate fixed by drying and treating with acetic acid and formalin as described in Fontana's method have been put away for fourteen days and the staining process then completed.

The results have been quite successful.

This may prove useful if a number of specimens are required for teaching purposes.

(4) The difficulty in distinguishing between Sp. pallida and Sp. microdentium makes the diagnosis of chancre of the lip, by microscopic methods alone, very difficult. If care be taken, however, to remove all traces of saliva and all surface spirochaetes the risk of this error will be reduced to a minimum. But as a rule patients with a chancre of the lip come for diagnosis and treatment when the chancre is fairly old, and after the more simple remedies have failed to heal it. By this time a Wassermann reaction will very probably settle the question.

(5) The combination of "Neokharsivan" and Mercurial/

Mercurial cream, as described in this paper, has so far proved a very satisfactory method of treatment.

(6) Re-infection after treatment with one of the more recent forms of the arsenical compounds e.g. neosalvarson or neokharsivan combined with injections of mercurial cream, is fairly common.

(7) The incubation period varies greatly in different cases but about 28 days is a fairly reliable average.

It may be as short as eighteen days and as long as forty days.

TABLE/

TABLE NO. 6.

Showing the number of films examined in each case before the Sp. pallida was found.
57 Cases of primary and secondary syphilis
Number of films examined before Sp. pallida found.

CASE NO.	DARK GROUND ILLUMINATION							SILVER METHOD						
	1	2	3	4	5	or more	Not found or uncertain	1	2	3	4	5	or more	Not found or uncertain
1		(doubtful case)					* 8							* 6
2	+								+					
3			+											* 2
4	+							+						
5	+													* 2
6	+							+						
7	+							+						
8	+								+					
9	+							+						
10	+							+						
11	+							+						
12	+							+						
(13)		(special case)												
(14)/		(special case)												

TABLE NO. 6 Continued.

CASE NO.	DARK GROUND ILLUMINATION							SILVER METHOD						
	1	2	3	4	5	or more	Not found or uncertain	1	2	3	4	5	or more	Not found or uncertain
(14)	(special case)													
(15)	(special case)													
16	+							+						
17	+								+					
18	+													* 2
19	+								+					
20	+							+						
21	+							+						
22	+							+						
23	+							+						
24	+													* 2
25	+													* 2
26	+							+						
27/	+							+						

TABLE NO. 6 Continued.

CASE NO.	DARK GROUND ILLUMINATION							SILVER METHOD						
	1	2	3	4	5	or more	Not found or uncertain	1	2	3	4	5	or more	Not found or uncertain
27	+							+						
(28)	"soft sore" - not included.													
29	+							+						
30	+													* 2
31	+							+						
(32)	special case													
33	+													* 2
(34)	special case													
35	+							+						
36	+							+						
37	+	(Throat)						+	(Throat)					
38	+							+						
39	+							+						
40/														

TABLE NO. 6 Continued.

CASE NO.	DARK GROUND ILLUMINATION							SILVER METHOD						
	1	2	3	4	5	or more	Not found or uncertain	1	2	3	4	5	or more	Not found or uncertain
40	+							+						
41	+							+						
42	+													* 2
43	+							+						
44	+													* 3
45	+							+						
46	+							+						
47	+							+						
48	+							+						
49	+													* 2
50	+							+						
51	+							+						
52	+							+						
53/														

TABLE NO. 6 Continued.

CASE NO.	DARK GROUND ILLUMINATION							SILVER METHOD						
	1	2	3	4	5	or more	Not found or uncertain	1	2	3	4	5	or more	Not found or uncertain
53	+							+						
54	+							+						
55	+							+						
56	+							+						
57	+													* 2
58	+							+						
59	"doped" chancre						* 2							* 2
60	+													* 2
61	+							+						
62	+							+						
63	+							+						
TOTALS 57	54		1				2	39	4					14
	55+						2-	43+						14

As shown in the above table when Sp. pallida was not found in the first film repeated examinations were made at intervals of one or two days and in the column headed "Not found or doubtful" the small number after the star denotes the number of examinations made.

I have much pleasure in thanking Captain James Miller, R.A.M.C.(T), for recommending this subject for a thesis, for his suggestions and guidance, and for the use of the Wassermann results.

LIST OF REFERENCES.

*1. Lustgarten - Wein. Med. Wchnschr. (1884) No. 47.

2. Schandinn and Hoffmann - Arb. a.d.k. Gsndhtsamte. (1905)

Bd. 22. p. 527. and in - Deutsch. Med. Wchnschr (1905)

Bd. 31 p. 711.

3. Noguchi - Journ. Exper. Med. (1912), XV. p. 466.

*4. Spitzer - Wein. Klin. Wchnschr. (1905)

*5. Sobernheim & Tomasczewski - München. Med. Wchnschr (1905)

6. Mulzar - *Berl. Klin. Wchnschr. (1905)

- Archiv. f. Dermat. U. Syph. (1906). 79.

*7. Tomasczewski - München Med. Wchnschr. (1906).

8. Noguchi and Moore - Journ. Exper. Med. (1913) XVII p. 232.

9. Metchnikoff and Roux - Ann. de l'inst. Pasteur (1903) XVII. p. 802

- (1904) XVIII p. i,6, & 657.

- (1905) XIX. p. 673.

10. Lassar - Berl. Klin. Wchnschr. (1903) p. 1189.

11. Neisser - Deutsch. Med. Schnschr. (1904) p.1369 & p. 1431

12. Nicolle - Ann. de l'inst. Pasteur (1903) XVII p. 636.

13. Noguchi - Journ. Exp. Med. (1912) XV. p. 90.

14/

14. Hoffmann - Deutsch. Med. Wchnschr. (1911) XXXVII p. 1546.

*15. Bordet and Gengou - Ann. de l'inst. Pasteur (1901) XV.

16. Wassermann, Neisser and Bruck - Deutsch. Med. Wchnschr. (1906) XIV p. 745.

17. Harrison - "Manual of Venereal Diseases" by Keogh, Melville etc. (2nd edition-1916-Oxford. Med. Publications).

18. Browning and Mackenzie - "Recent Methods in the Diagnosis and treatment of Syphilis" (London - 1911) p. 23.

19. The Wassermann Test. Interim report of Special Committee of Medical Research Committee. published by Darling. London - 1918.

20. Harrison - "The Diagnosis and treatment of Venereal diseases in general practice" 1918- Oxford Med. Publications).

21. Modified Fontana's stain - Brit. Med. Journ. Dec. 18th 1915.

22. Hoehne - "Serum Diagnosis of Syphilis" by Noguchi. (2nd edition -1911- Lippincott & Co. Philadelphia). p. 116.

23. Hoehne - "

24. Noguchi - "

25. Kolmer - Infection, Immunity & Specific Therapy. (2nd edition 1918 - Philadelphia) p. 492.

26. Muir and Ritchie - "Manual of Bacteriology" (6th edition - 1913). p. 116.

27. Phillips and Glynn - Brit. Med. Journ. Nov. 11th 1911.

28. Noguchi - Journ. Exper. Med. (1912) XV. p. 466.

29/

29. Levaditi and Stanesco - Compt. rend. Soc. de biol. (1909) LXVII. p. 188.

30. Harrison - "Diagnosis and Treatment of Venereal Disease in General Practice". p. 266.

31. Hoffmann and Prowazek - Centralbl. f. Bakteriol. (1906) Ite. abt. Orig. XLI. p. 741.

32. Levaditi and Stanesco - Compt. rend. Soc. de biol. (1909) LXVII. p. 189.

33. Noguchi - Journ. Exper. Med. (1912) XV. p. 81.

34. Noguchi - Journ. Exper. Med. (1912) XV. p. 81.

35. Ellermann - Centralbl. f. Bakteriol. Orig. (1904) XXXVII. p. 729.

36. Weaver and Tunnicliff - Journ. Infect. Diseases. (1905) ii. p. 446.

37. Muhlens - Deutsch. Med. Wchnschr. (1906) XXXII. p. 797.

38. Hutchinson. J, - "Syphilis" (1909 - London). Chap. XVII.

39. Muir and Ritchie - Manual of Bacteriology. (6th edition - 1913). p. 267.

40. Special Report Series, No. 19. of Special Committee of Medical Research Committee - 1918. p. 47.

The references, which are marked with a star, have not been personally confirmed.

D I A G R A M S

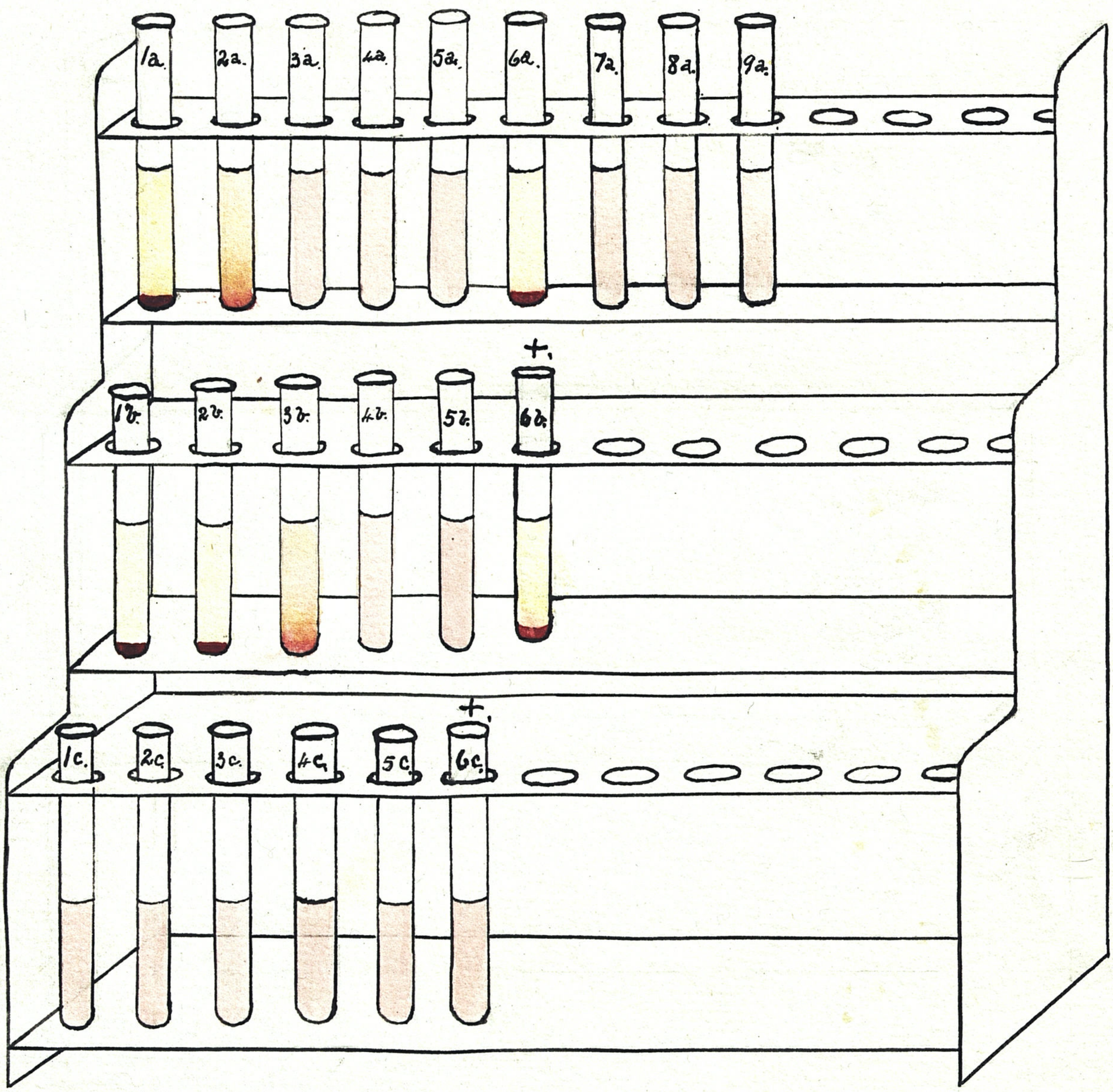
and

P H O T O G R A P H S

Two Boxes of slides accompany the Thesis illustrating the fact that the Silver Stain fades rapidly.

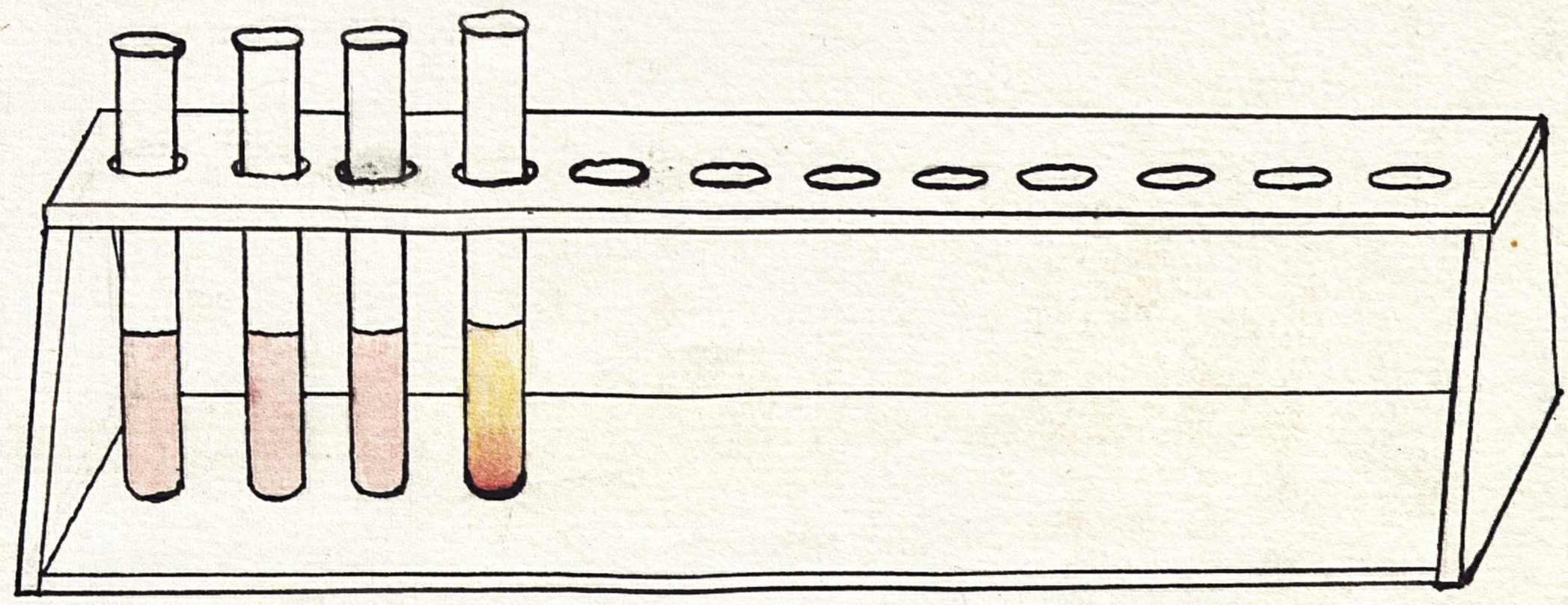
Many of the photographs that are here shewn were taken from some of these slides.

FIGURE Nº 1.



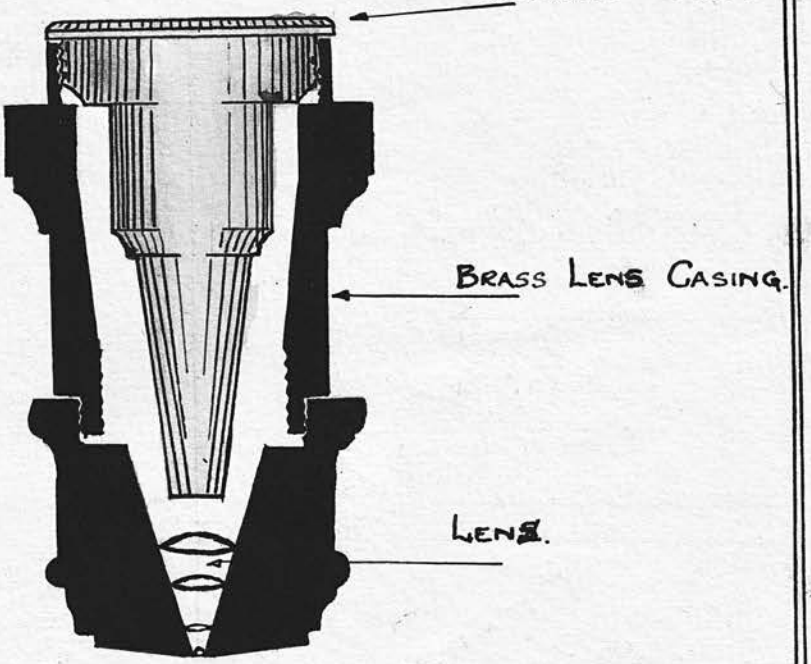
WASSERMANN STAND showing 5 patient's sera and Controls.

FIGURE № 2.



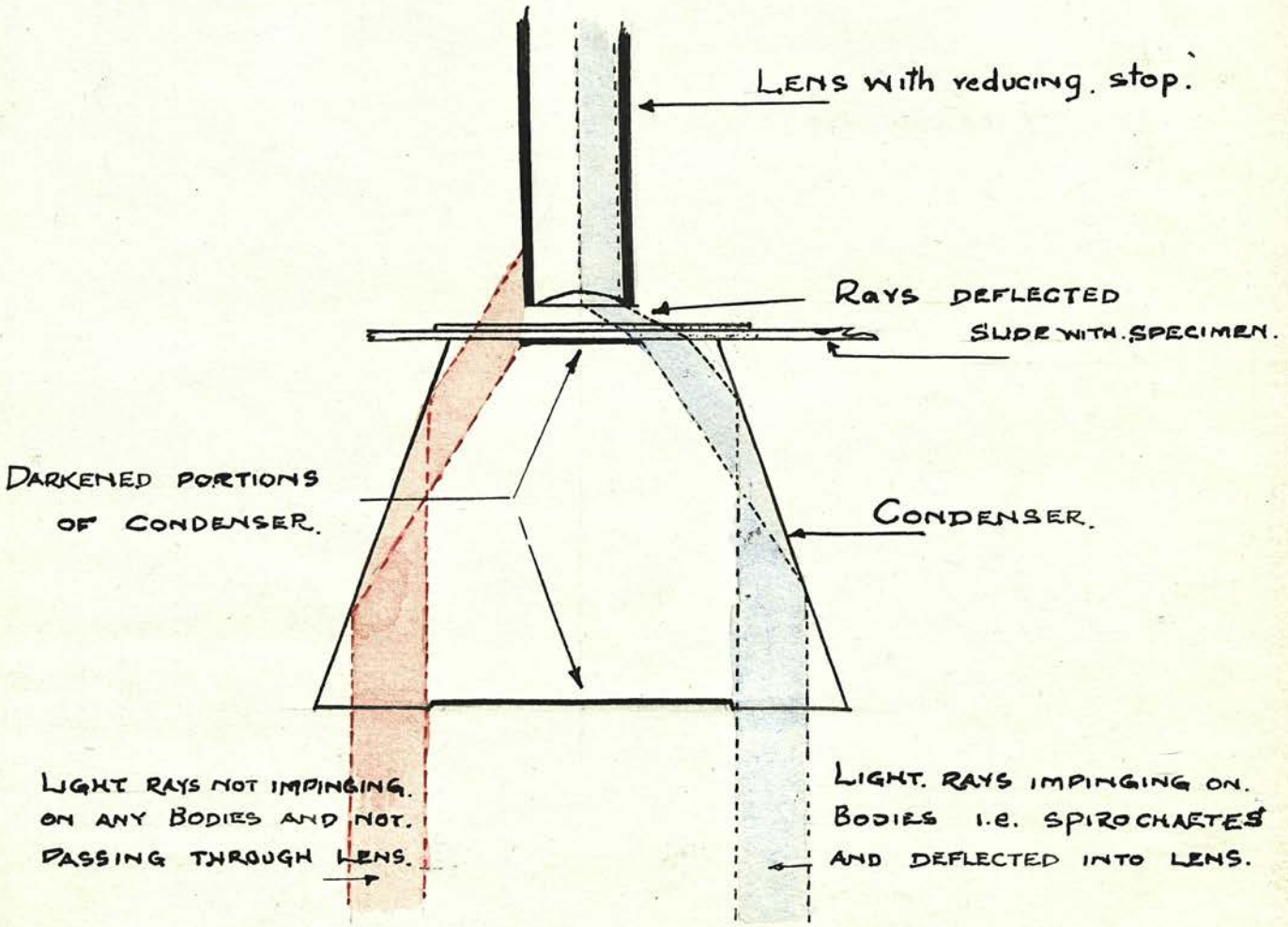
STAND for finding M.H.D. of Complement and Immune Body.

FIGURE Nº 3.



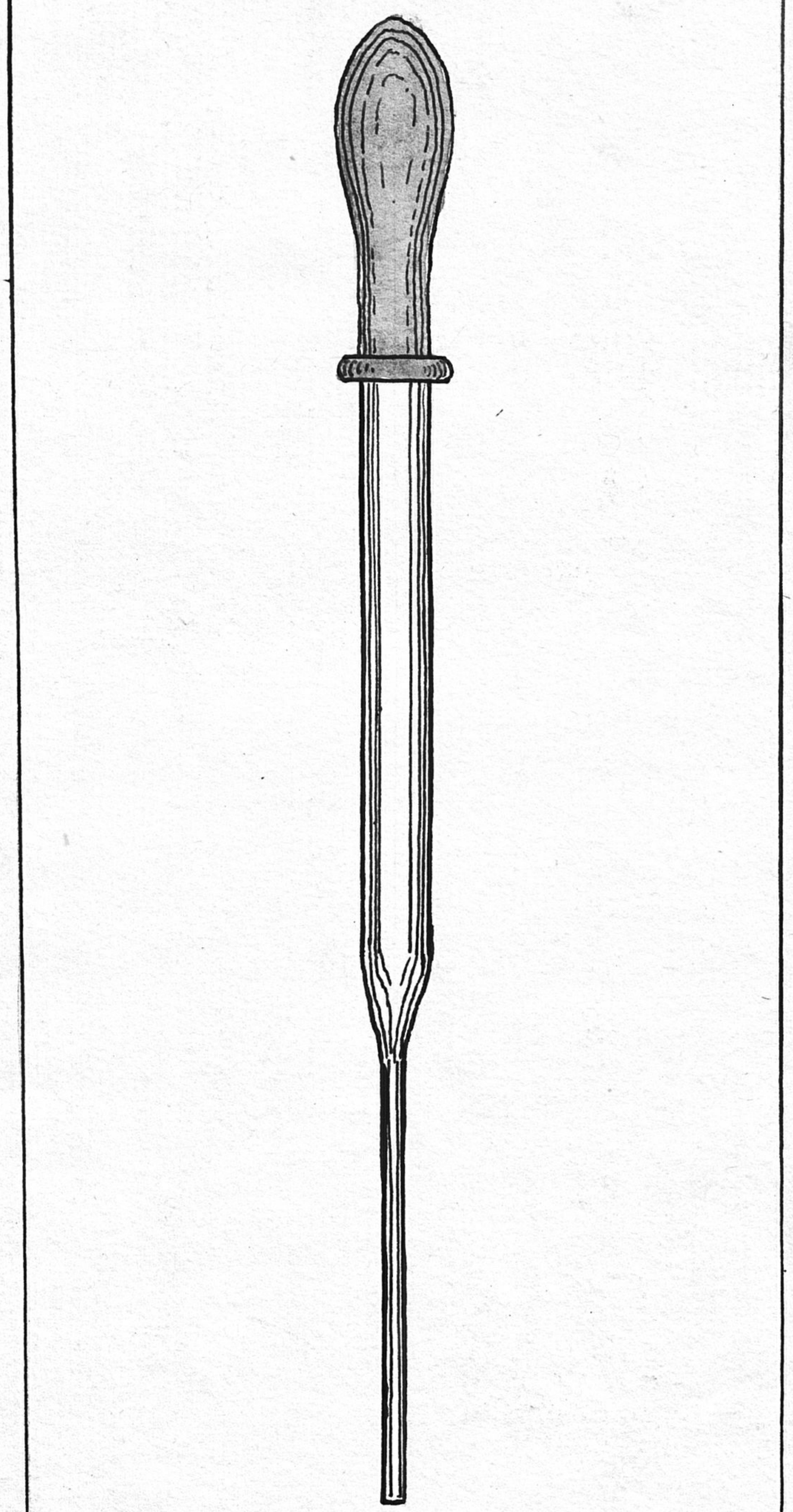
SECTION OF LENS
SHOWING. REDUCING STOP.

FIGURE Nº 4.



WATSON'S. DARK GROUND CONDENSER

FIGURE Nº 5.



CAPILLARY PIPETTE

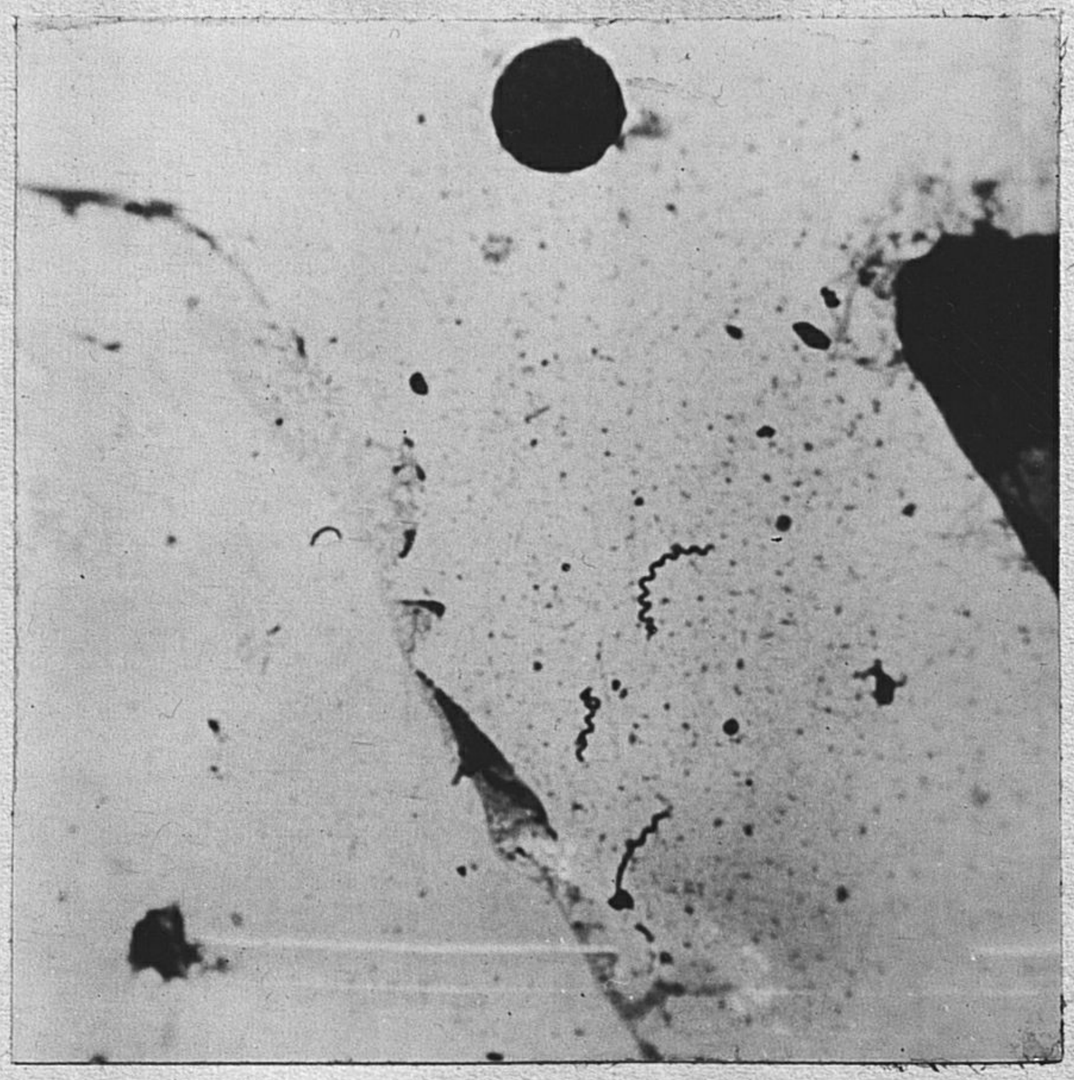


Photo No. 1 Sp.pallida. (silver stain - X 1000)

Characteristic coils retained. Comparison with red cell shows seven coils to the diameter of the cell.

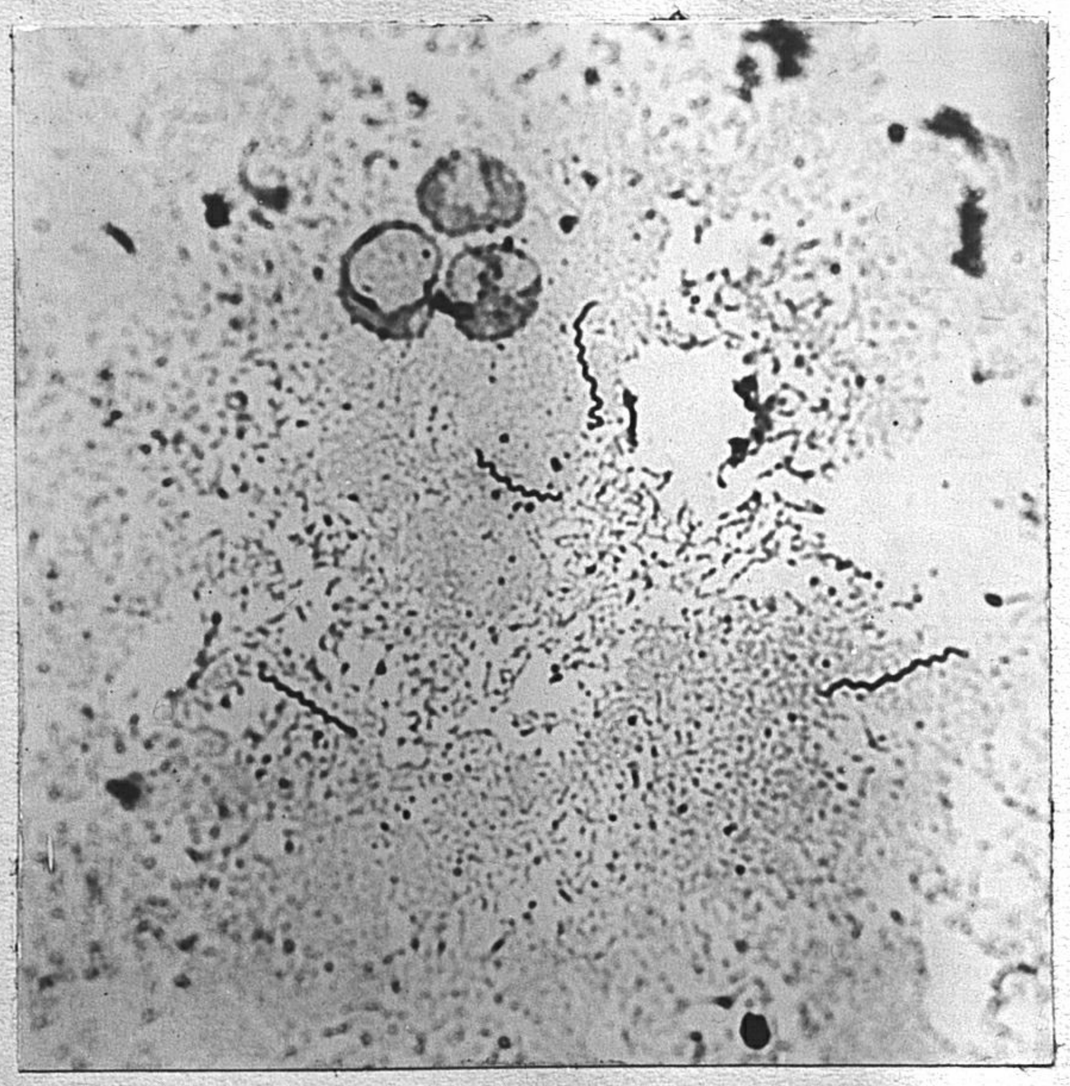
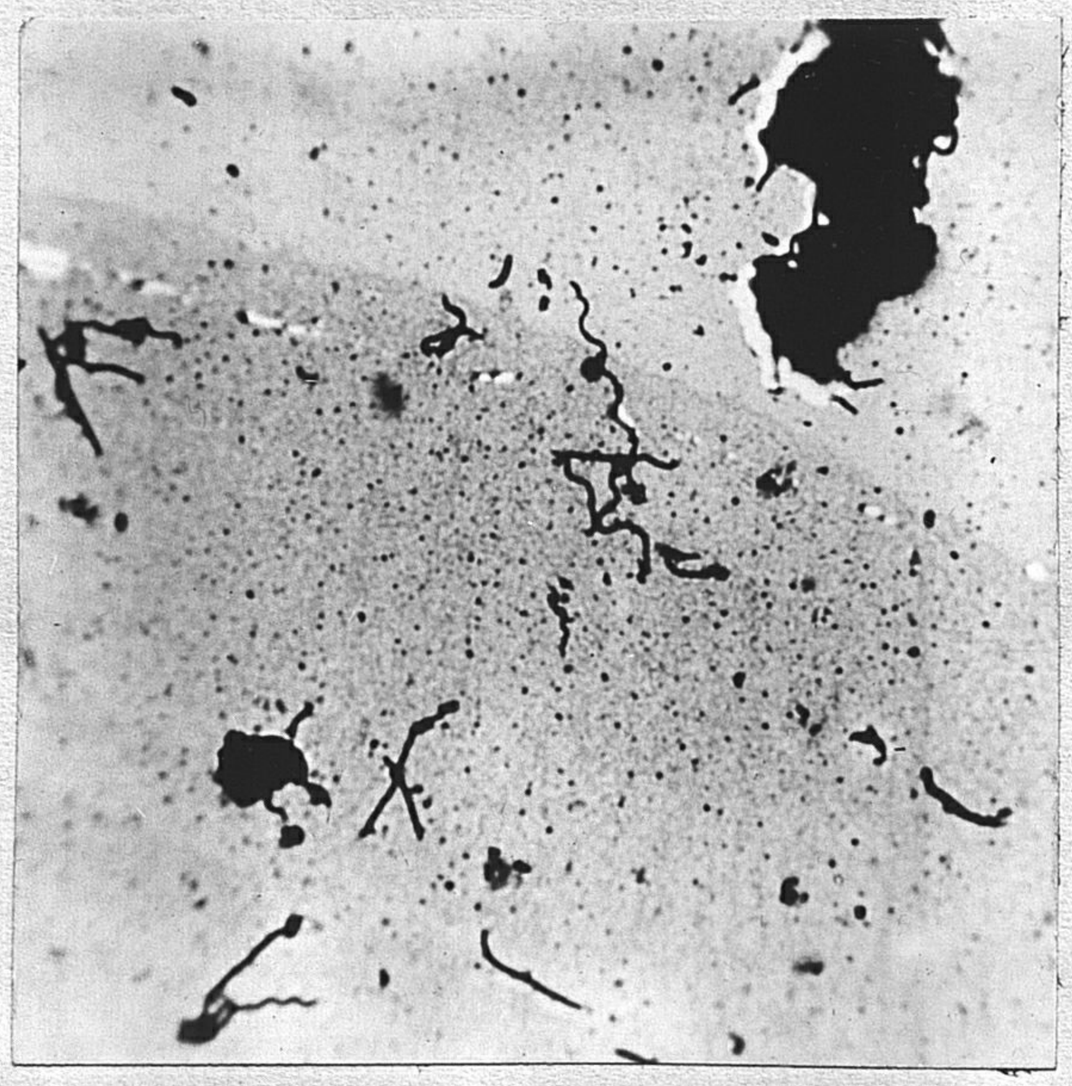


Photo No. 2. Sp.pallida. (silver stain - X 1000)

Four typical Sp.pallida. In this case(No.63) the dark ground method revealed the presence of a great number of spirochaetes. Specimens taken at same time.



Duplicate Photo No.6.

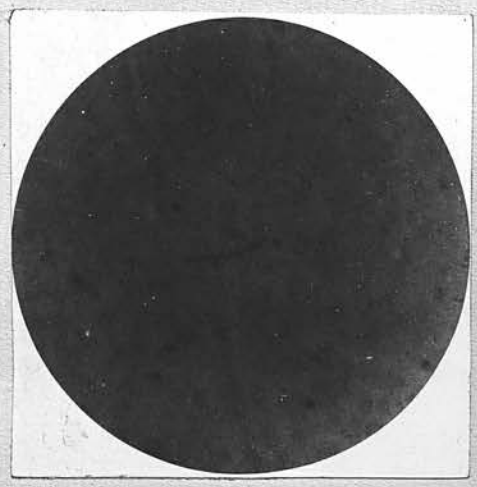


Photo No. 3. Sp.pallida (silver stain - X 1000)

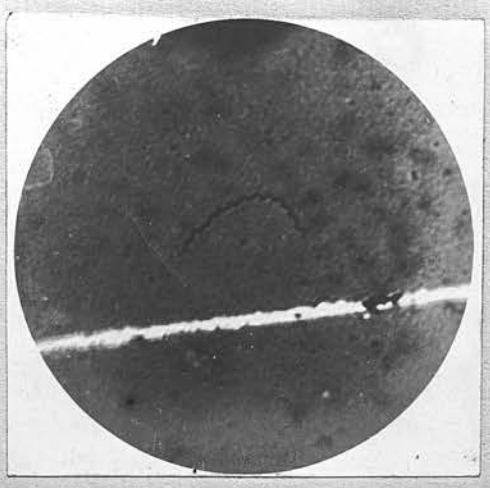


Photo No. 4. Sp.pallida (silver stain - X 1200)

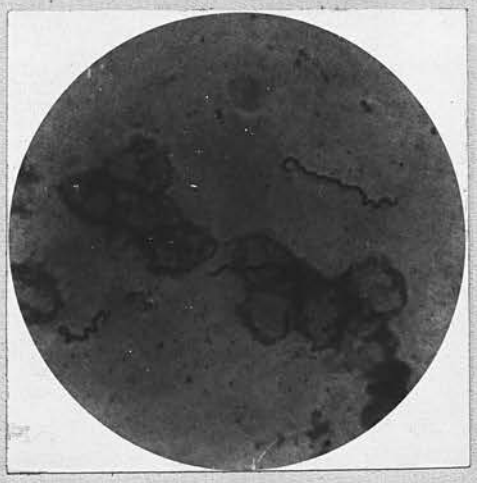


Photo No 5. Sp.pallida (silver stain - X 1200)

Showing how in some films Sp.pallida may loose its characteristics as a result of the methods of preparation.

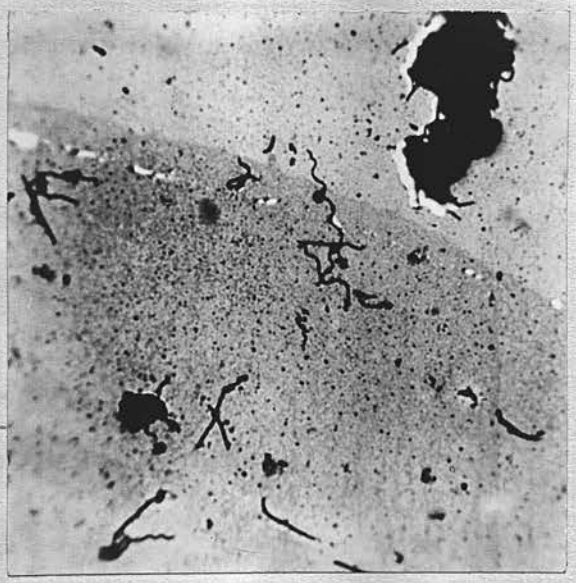


Photo No. 6 Sp.refringens. (silver stain - X 1000)

Showing one typical Sp.refringens with wide wavy coils and several others which have lost their typical appearance and look like thick straight rods; the effect of staining on most spirochaetes.

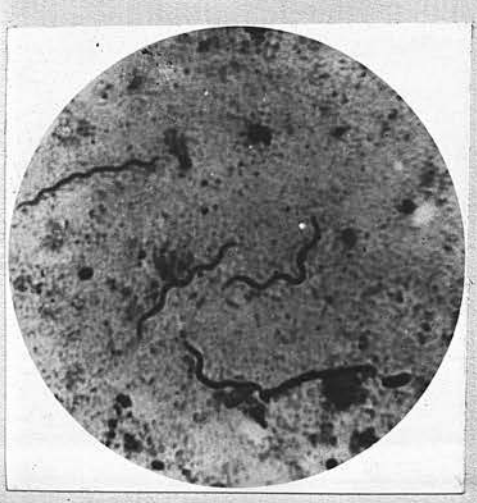


Photo No. 7 Sp.refringens. (silver stain - X 1200)

Showing how their appearance may be altered by staining process.

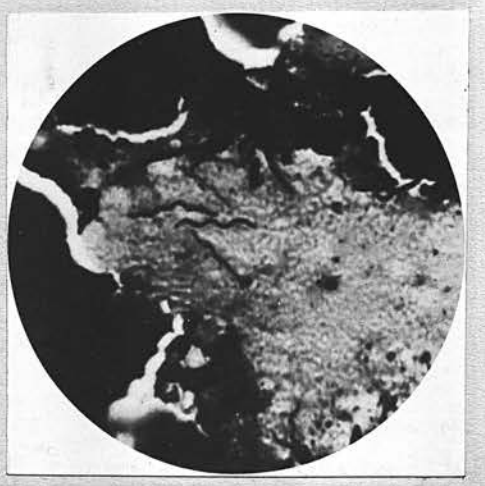


Photo No. 8 Sp.balanitidis. (silver stain - X 1200)

One typical Sp.balanitidis - short thick spirochaete with two or three coils - seen between two other spirochaetes.

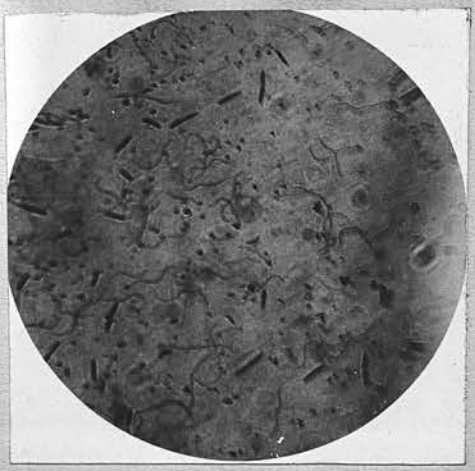


Photo No. 9. Spirochaetes and B.fusiformis of Vincent's Disease (Neisser's stain - X 600)

Taken from case No. 14. These spirochaetes have large wave-like coils.

Photo No. 10. Spirochaetes and B.fusiformis of Vincent's Disease (Gram's stain - X 600)

(Case No. 14) These Spirochaetes are associated with large fusiform bacilli.

TELEPHONE Nº 8020.

University of Edinburgh
New Buildings

PROFESSOR HARVEY LITTLEJOHN,
DEAN OF THE FACULTY OF MEDICINE.

The University New Buildings.
Edinburgh 22nd Oct 1918

Professor Ritchie

Theses by the under-mentioned are sent for examination and report:-

Capt A. G. Biggam, R.A.M.C.
Capt. W. A. Young D.S.O., R.A.M.C.
(Box of Slides with latter)